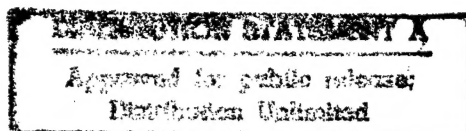191015

USSR Report

SPACE BIOLOGY AND AEROSPACE MEDICINE

No 1, JANUARY-FEBRUARY 1986

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USSR REPORT

SPACE BIOLOGY AND AEROSPACE MEDICINE

No. 1, January-February 1986

CONTENTS

PROSPECTS FOR USING ULTRAVIOLET RADIATION IN LONG-TERM SPACEFLIGHTS

[Article by N. Ye. Panferova]

[English abstract from source] The data concerning UV-effects
on the human body and the environment are reviewed as applied
to long-term flights. It is concluded that UV-radiation can
be used in long-term spaceflights in view of its vitamin-
forming, desensitizing, bactericidal and supporting properties
to improve the environment and to prevent adverse effects of
spaceflight factors.

[Text] Essentially artificial sources of light wanting in UV radiation (UVR)
are used in flight to illuminate manned compartments for cosmonauts. As we
know, UVR is one of the factors that is essentialy to normal vital functions
of man. UVR elicits changes in molecular structures of cells, in particular,
nucleoproteins, amino acids, carbohydrates and other biological constituents.
This is associated with formation of biologically active substances, such as
kinins, arachidic acid, prostaglandins E_2 and $F_{2\alpha}$ [43, 49], pyrimidine dimers
[38]; it increases activity of enzymes involved in redox processes in the
system of cellular respiration on the level of aerobic (dehydrases) and
anaerobic (cytochromoxidases) parts. As a result, there is an increase in
intensity of redox processes in tissues of the brain, liver, heart and kid-
neys [28].

By affecting directly cutaneous nerve endings and, through the formed meta-
bolites, nerve endings of other organs, UVR elicits a tonic reflex effect.
The mechanism of general stimulating action of UV rays is apparently analogous
to that of nonspecific therapy--autohemotherapy, implantation of foreign
tissue, etc. [31].

In accordance with the decision of the International Commission for Illumination
adopted in 1963, UVR was divided into three regions according to intensity of
its biological effects: A, B and C. Region A refers to radiation at wave-
lengths of 320-400 nm, region B--280-320 nm and region C, less than 280 nm.

UVR in the C range elicits effects on the level of proteins of cell nuclei,
and it is notable for high bactericidal activity. Radiation in this range

is virtually wanting in sunrays reaching earth's surface, since it is absorbed by the atmosphere. For this reason, artificial sources are used to produce it on earth, i.e., bactericidal lamps. The rays in this range are an undesirable "impurity" in UVR sources intended for irradiation of man. Their levels should not exceed 5% of the total flux.

Medium-range radiation (region B) interacts mainly with molecules of cell protoplasm proteins. It is believed that protoplasm proteins perform the function of additional filters, protecting cell nuclei from damage [52]. The superficial layer of skin is characterized by a low coefficient of penetration for UV rays. Nevertheless, UV rays in the B range can penetrate into the skin to a depth of 1 mm [30]. Skin reddening--erythema--appears as a result of exposure to large doses of medium-range radiation. The latter activates production of vitamin D in the skin.

The rays in the long-wave region of UVR have the capacity to penetrate the deepest into integumental tissues. In spite of this, it was believed for a long time that region A rays are biologically inactive, and for this reason their biological effects have been studied less. At the present time, it has been established that rays in this part of the solar spectrum are notable, in large doses, for high capacity to stimulate melanin production with the involvement of melanin-stimulating hormone, they have a tonic effect on the central nervous system, adrenals, cardiovascular system, etc.

The nature of reactions to UV is also determined by intensity and mode of exposure. By changing the frequency, duration and intensity of exposure to radiation one can induce opposite effects. Low doses of UVR increase viability and intensity of cell reproduction and high ones, depress this process [27].

We should include the existence of a prolonged (up to 3 weeks) aftereffect period among the distinctions of biological effects of UVR [17].

In the course of evolution, living organisms developed a number of mechanisms against intensive UVR. They include increase in thickness of the epidermis and pigmentation of the skin. In addition, the top skin layers contain urocanic acid, which is a natural screen that absorbs rays at wavelengths of 290-310 nm [45]. When exposed to UVR, the thickness of the epidermis increases due to increase in intercellular fluid in the skin of the exposed region. The rate of cutaneous cell division in this region increases about 3 days after irradiation. As a result of formation of new cells, the thickness of all skin layers, with the exception of the pigment layer, increases. Thickening of epidermal layers is the most effective protection against the deleterious effect of UVR. Skin pigmentation has a less marked protective effect. Thus, the protection index (ratio of erythemic sensitivity of sunburned to nonsunburned skin) is 2-3. The protection index of sunburned skin combined with thickening of the cornified layer increases to 60.

The energy of UV rays is measured in the following units: radiation flux in W, radiation force in W/sr, radiation power density in W/m^2 and radiation level in J. Relative biological units have gained wide use to characterize erythemic, bactericidal, pigment- and vitamin-producing activity of UVR.

The intensity of the most active monochromatic radiation is taken as the unit. Activity of the rest of the radiation is expressed in relation to this unit.
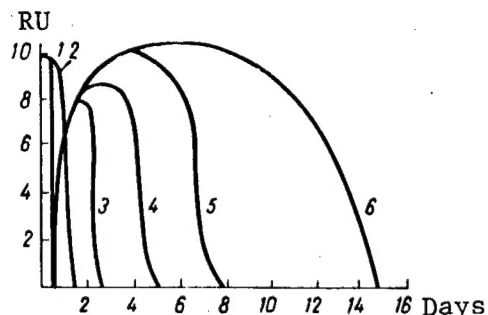
Figure 1.
Time of onset and disappearance of erythema due to UVR [32]
X-axis, time of appearance and disappearance of erythema (days); y-axis, intensity of erythema (in relative units--RU).
1, 2) with low and high doses of long-wave UVR (320-400 nm)
3, 4) same with short-wave UVR (less than 280 nm)
5, 6) same with medium-wave UVR (280-320 nm)

Figure 2.
Erythemic activity of UVR as a function of wavelength according to data of different authors [21, 36, 39, 54]
X-axis, wavelength (nm); y-axis, erythemic activity (in relative units--RU). 1-4--standard curves (sources [36], [21], [39] and [54], respectively)

UVR in all ranges has bactericidal activity, but the maximum effect is referable to short-wave rays at wavelengths of 253-257 nm. With increase in wavelength, bactericidity decreases dramatically. For example, it constitutes 0.25 RU [relative units] at 220 nm, 1.0 at 254 nm, 0.87 at 270 nm, 0.06 at 300 nm and 0.0001 at 400 nm.

UVR in all ranges has erythemic activity. Maximum activity is referable to medium-wave UVR, short-wave UVR has lower but rather marked activity and long-wave, mild activity. Erythema presents qualitative distinctions, depending on the spectrum of UV rays (Figure 1). It is less intensive, has a shorter latency period and persists for a shorter time with short-wave UVR than erythema associated with the medium-wave range [37]. It is believed that the erythema that develops from long-wave UVR is nonspecific, since it is produced by dilatation of vessels and perivascular edema due to increased heat production in the skin, rather than by formation of metabolites [51]. This form of erythema is formed during irradiation and persists from a few min to 24 h, depending on the dosage (Figure 2). The erythemic aftereffect of long-wave UVR is not associated with intensified skin cell division or thickening, which is typical of medium-wave UVR.

The mechanism of production of UVR-specific erythema has not yet been definitively identified. It is believed that metabolites are involved in its production, in particular, histamine, kinins, prostaglandins E_2 and F_{2a}, products of nucleotide metabolism [51].

There are data to the effect that the correlation of erythemic activity of monochromatic UV rays is rather stable in different individuals. This made

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it possible to express UVR erythemic activity as a function of wavelength in the form of a curve, which is presently adopted as the standard (see Figure 2). The curve served as the basis for biological erythema units. The power of UV flux at the wavelength that is the most active for erythema is taken as the basic unit. Most authors believe that rays at a wavelength of 297.6 nm have such activity. UVR of 1 W at wavelength of 297.6 nm within a 1° solid angle is taken as 1re [roentgen equivalent] [21] or 1 RU [36]. If the energetic and biological characteristics of monochromatic rays in mixed flux are known, one can calculate erythemic activity of the entire flux, expressing it in biological units (re or RU).

Thus, the data on magnitude of overall radiation flux or UV ray power density in energy units are not informative enough as to the biological activity of this flux. Thus, according to the standard curve, at the same energy of radiation at a wavelength of about 297 nm, there will be prevalence of maximum erythemic effect, whereas the erythemic acti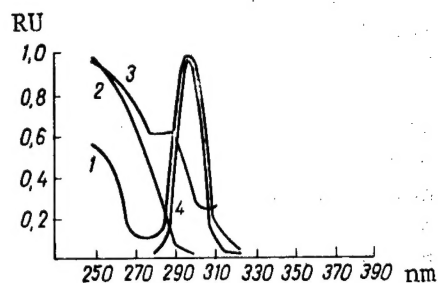vity of a radiation flux at wavelengths of 280 or 315 nm will be close to zero. However, there are a number of studies, in which different findings were made (see Figure 2) concerning erythemic activity as a function of UVR wavelength [37, 39, 54]. This led some authors to adopt a skeptical attitude about the informativeness of relative biological units.

The question of intensity of erythemic activity of UVR at different wavelengths is of definite interest to both practical and theoretical space medicine. It is important both for investigation of mechanisms of action of UVR on living organisms and to determine the biological effectiveness of UV sources used for irradiation. Apparently, special investigations must be conducted to define erythemic activity as a function of wavelength.

The threshold of erythema sensitivity or minimal erythemic dose (MED) is used to characterize skin sensitivity to UVR. MED is the minimal amount of UVR eliciting erythema. MED is expressed in joules per square meter. It ranges from 60 to 600 J/m^2, depending on individual distinctions of tested subjects, with exposure to UVR at a wavelength of 297.6 nm. But, since it is not always possible to measure exactly the specific power of individual monochromatic rays from the source, MED is often expressed in minutes in medical practice. Consideration is given to the fact that the amount of delivered energy is proportionate to duration of irradiation in the case of constant spectral composition, power and distance from source to irradiated surface.

The skin's sensitivity to erythema increases when man spends a long time in an environment with a shortage of UVR. It is believed that there is a direct relationship between erythemic sensitivity of the skin and duration of such conditions. Sensitivity is higher in the winter than in the summer; it is higher in individuals who have lived in Arctica for at least 5 years than in those who have spent less than 1 year there [24].

UV erythema is a complex vegetovascular reaction that is closely related to metabolic processes in the skin, nervous system function and state. The erythemic reaction is attenuated or is not manifested at all in patients with involvement of the hypothalamus, impaired conduction in the spinal cord and peripheral nerves [4, 9, 22].

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Erythema due to UVR is viewed as an undesirable phenomenon related to over-dosage of UVR and destruction of skin structures. For this reason, sub-erythemic doses are recommended when using UVR for preventive purposes.

The antirickets effect or vitamin D producing effect is used as a criterion of beneficial action when using artificial UVR sources for prophylactic purposes [7]. Man requires UVR in a dosage of 45 MED/year over a skin area of at least 500–600 cm^2 to prevent development of vitamin D deficiency. This is not a large dose. In southern regions, man can be exposed to a total of 630 MED UVR per year [6, 8].

The results of an investigation revealed that 1/8–1/10 MED, or 30–40 J/m^2, with exposure to 297.6 nm waves, is the minimal or threshold dose for the antirachitic effect. Lower doses were not observed to have a preventive effect.

Studies on animals revealed that use of threshold doses is not always reliable; for this reason, it is recommended to increase the radiation dose to 1/2–3/4 MED for guaranteed protection against avitaminosis [19].

The vitamin-producing effect of UVR is also related to UVR wavelength [1]. Maximum activity is observed at 280 nm. It diminishes at 270 and 315 nm. A dosage of 420 mJ of medium-wave radiation at 297.6 nm, over a skin area of 200 cm^2, is sufficient to treat rickets [40].

A comparison of the antirachitic effect of UVR and intake of vitamin D re-vealed that suberythemic doses of UVR are more effective in prevention of osteoporosis than vitmain D. The greatest effect was obtained with a combina-tion of vitamin D and UVR in a dosage of 1/8 MED [15]. Production of vitamin D from the provitamin 7-dehydrocholesterol (7-DCS) is a specific effect on the skin of medium-wave radiation.

Control of vitamin D production in the body is a complicated process, in which many organs and systems are involved. Evidently, this process begins with control of 7-DCS content in the skin. There are receptors in skin fibro-blasts and keratinocytes which, apparently, affect 7-DCS content of the skin [42]. Previtamin D$_3$, which is fromed from 7-DCS under the influence of UVR, is subject to thermal isomerization in the skin, with formation of vitamin D$_3$. The latter has high affinity for vitamin-binding blood protein, and it is gradually flushed from the skin into the blood [44], then passes with the latter into the liver. Vitamin D$_3$ in itself has little biological activity. Its metabolites have high activity. In the liver, 25-hydroxycholecalciferol is synthesized from vitamin D$_3$. From the former, 1,25-dehydroxycholecalciferol (1,25-DCC), 24,25-dihydroxycholecalciferol (24,25-DCC) and 1,24,25-trihydroxy-cholecalciferol (1,24,25-TCC) are formed in the kidneys. The formed meta-bolites are an active part of the system that provides for Ca homeostasis in blood. Metabolite 1,25-DCC is localized in cell nuclei. It is similar to hormones in its action. This metabolite stimulates production of calcium-binding protein in the intestine and thereby is instrumental in Ca absorption in the form of phosphorus compounds from the intestine into blood. As a result, Ca and P levels rise in blood and extracellular fluid. In addition, the same metabolite causes elevation of blood Ca level to physiological values as a result of Ca adsorption from bone. The level of 1,25-DCC rises in the presence of hypocalcemia. With normal and high Ca levels in blood and

interstitial fluid there is predominant production of 24,25-DCC in the kidneys. Normally, the concentration of the latter metabolite in blood is 100 times higher than that of 1,25-DCC. It is assumed that 1.25-DCC increases Ca adsorption from bone when its blood level is low. Adsorption of Ca by bone is increased by 24,25-DCC when its blood level is high [46]. The functions of vitamin D_3 metabolites have not yet been definitively identified. As we have already mentioned, pigmentation of the skin limits the deleterious action of UVR, but at the same time it apparently lowers the intensity of vitamin D production [53].

UVR causes pigmentation of the skin and, depending on intensity of radiation and wave length, it presents qualitative differences. The long-wave range elicits two types of pigmentation: immediate and persistent. Immediate pigmentation is an emergency mechanism of protecting the skin against the deleterious effect of UVR. It is attributable to oxidation of colorless promelanin to melanin under the influence of UVR. Immediate pigmentation disappears within 1–1.5 h. With higher dose rate (over 17.7 ± 8.0 J/cm^2), immediate pigmentation changes to persistent form [45], which may last for more than a year. Production of persistent pigmentation is related to activation of melanogenesis and melanin production. Special cells, melanocytes, which are situated in the basal skin layer, perform the function of melanin production. These cells secrete melanin granules which penetrate, through melanocyte processes, into the epidermis and change its color. Melanin is formed from the amino acid, tyrosine, with involvement of the enzyme, tyrosinase. Tyrosinase activity is closely related to melanin-stimulating hormone, which is secreted by the intermediate lobe of the hypophysis.
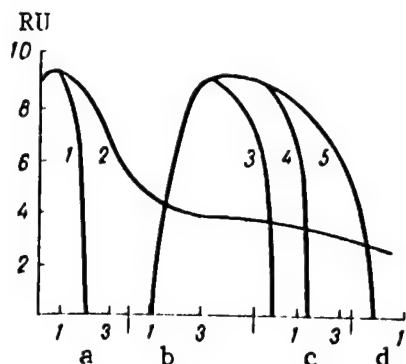
Figure 3.
Pigment-forming activity of UVR [32]. X-axis, time of appearance and disappearance of pigmentation (a--in hours, b--in days, c--in months, d--in years); y-axis, intensity of skin pigmentation (relative units)
  1, 2) low and high doses of long-wave UVR (320–400 nm)
  3) short-wave UVR (under 280 nm)
  4, 5) low and high doses of medium-wave UVR (280–320 nm)

Medium- and short-wave UVR in doses exceeding MED also activates melanogenesis. In this case, pigmentation appears in about 24 h and persists for 2 to 12 months, depending on radiation dose (Figure 3). The protective effect of skin pigmentation against the deleterious action of UVR is more marked with use of medium- and short-wave UVR than long-wave radiation. This is related to the fact that with exposure to UVR of zones B and C in doses exceeding MED there is an increase in thickness of skin layers. There is summation of the protective effects of pigmentation and thicker epidermis.

UVR activates the defense mechanisms of the human body, in particular, nonspecific immune defense, and there is elevation of levels of properdine, complement, γ-globulin fraction in blood, with increase in phagocytic activity of leukocytes [3]. UVR enhances adaptability to adverse environmental factors. Activation of immune protection increases constitutional resistance to adverse environmental factors, including infectious ones.

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UVR accelerates resorption of inflammatory foci [3], increases histaminase production [10], survival rate of infected mice [26, 41], birthrate, and lowers the incidence of stillbirths [14].

Suberythemic doses of UVR enhance resistance to neoplasms. However, a 2.3-fold increase in tumor growth has been observed with 10 MED [16]. Chronic exposure to suberythemic doses had no carcinogenic effect on mice [13, 35].

Three methods [25] of using medium-wave UVR have gained the widest use in medical practice:

> Delivery of suberythemic doses of 0.5-0.7 MED; this method is used to prevent vitamin deficiencies in individuals who are deprived of UVR for long periods of time. It has gained use in schools and industry. Cumulative UVR constitutes about 144 J/m^2.

> Exposure of different parts of the body. This method develops mechanisms that counteract development of erythema.

> Multiple delivery of radiation in increasing doses, from sub-erythemic to above erythemic; this method has a conditioning effect that is instrumental in developing adaptive mechanisms of the body in relation to environmental conditions.

The dosage delivered per session ranges from 60-300 to 300-1500 J/m^2, depending on the individual's skin sensitivity [25].

Medium-wave UVR in doses exceeding MED elicits change in cells of the skin, vessels and connective tissue. In the case of chronic irradiation, there is about 3-fold increase in thickness of the cornified skin layer. The skin acquires uneven pigmentation and thickness, loses its elasticity, turgor, capacity to bind water. Skin vessels open into the atrophied connective tissue. As a result, there is development of carcinoma [2].

The eyes are the most sensitive to short-wave UVR in the range of 265-280 nm. Maximum eye sensitivity is referable to a wavelength of 270 nm. The threshold of photokeratitis-inducing effect is 40 J/m^2 at 270 nm and 50 J/m^2 at 280 nm [50]. The opinion is held that these threshold levels of UVR for production of photokeratitis are underestimated, and it was decided to raise them by 15%.

If UV rays hit the eyes in a dosage of over 25 J/m^2 visual acuity diminishes. The latency period of photokeratitis development may range from 30 min to 24 h. Absence of adaptation to repeated exposure is a distinction in the eye's reaction to UVR. The lens has increased capacity to absorb the long-wave range of UV. As a result, with acute irradiation there may be fluorescence of media of the eyes and lens, which is associated with loss of clear vision.

It is believed that chronic exposure to high doses of UVR in the wave range of 300-400 nm could serve as the cause of cataract development [32].

However, proper dosage of UVR and use of protection render use of UVR ab-solutely safe and beneficial to the human body.

A shortage of natural sunlight and UVR creates conditions for development of hypovitaminosis D, osteoporosis and erythema of the skin upon contact with UVR. Some authors consider the consequences of UVR deficiency to be diseases of civilization [33].

Long-term stays in a closed environment, in particular, like those of spacecraft operators, are related to a dramatic shortage or absence of UVR.

At the present time, it is believed that it is necessary to produce an environemnt aboard spacecraft including factors that make up the essential elements of man's natural habitat [5, 29]. Apparently, UVR should be included among these factors.

It is to be expected that UVR will be one of the important elements in development of preventive measures to enhance general resistance and work capacity of cosmonauts, and to improve living conditions in a spacecraft.

When settling the question of exposure of operators to UVR, one must take into consideration the specifics of spaceflight conditions. Apparently, the experience gained in use of UVR for preventive and therapeutic purposes on the ground cannot be unambiguously extrapolated to a spacecraft.

The following aspects of UVR action may serve as indications for its use during spaceflights: improvement of environment, conditioning of the body in order to increase work capacity and resistance to adverse spaceflight factors, prevention of disturbances in mineral metabolism during spaceflights, for therapeutic purposes with onset of pyogenic diseases of the skin, diseases with concomitant allergic component, for desensitization to allergens, etc.

Monotony of ambient conditions (in particular, the microclimate) is one of the adverse factors of spaceflights. Use of UVR during long-term missions may be promising, not only as a means of decontaminating the environment, but as a factor that offers diversification to the body and reduces the monotony of spacecraft environment factors.

One of the main consequences of man's exposure to spaceflight factors is impairment of mineral metabolism, in particular that of Ca. In this regard, it becomes necessary to pursue investigations to determine the role of UVR deficiency in flight in development of these disturbances. It is also important to determine the extent to which UVR could have a corrective influence on mineral metabolism under these conditions.

There have been virtually no studies in this direction (either during spaceflights or with simulation of their factors on the ground). There are only a few works shedding light on the effect of vitamin D metabolites on phosphorus-calcium metabolism in animals submitted to hypodynamia. It was established that 1,25-DCC content of serum, kidneys, intestine and bones diminishes when mobility of rats is restricted. At the same time, there is increase in renal level of 24,25-DCC [29].

General resistance of the body, its immunological reactivity, diminishes during spaceflights; there is development of sensitization to allergens

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of the principal representatives of the body's microbial autoflora [20]. At the same time, there is increase in bacterial contamination of the air environment of manned modules of the craft and skin [17, 18, 23].

As we have already mentioned, the entire spectrum of UV rays has bactericidal properties. However, maximum activity is referable to short-wave UV radiation, i.e., at wavelengths of less than 280 nm, exposure to which is undesirable for humans. Apparently, one can use sources of medium- and long-wave UVR to lower bacterial contamination of the skin.

Apparently, special studies must be conducted on use of UVR for the purpose of prevention of development of the above-mentioned phenomena.

Short-wave UVR has mutagenic properties. The question of variability of microorganisms under the effect of UVR and its ecological implications also require special investigation.

There are many polymers and synthetic materials within the spacecraft. UVR is a chemically active factor which could alter their structure by affecting surrounding materials (particularly polymers). This could lead to production of undesirable substances in manned modules. This aspect of UVR effects also requires special study.

The sensitivity of human skin to UVR changes under the effect of various environmental factors, temperature, humidity and mobility of air. It can be expected that redistribution of blood-filling in different parts of the skin could alter the MED. The results of our investigations revealed that sensitivity of the skin of the upper half of the body to medium-wave UVR may change during short-term antiorthostatic hypokinesia.

We are not quite clear as to the optimum range of UV wavelengths that should be recommended for cosmonauts during spaceflights. Soviet preventive medicine recommends the use of medium-wave UVR when there is a shortage of UV [6, 8, 11, 12, 14, 21]. However, many researchers, particularly foregin ones [34, 47, 51], have voiced the fear that medium-wave UV rays could cause adverse changes in the body, particularly in the case of overdosage. For this reason, these researchers recommend broader use of long-wave UVR. In addition to the spectral composition of UVR, it is necessary to settle the question of dosage, mode, frequency and duration of exposure.

The problem of furnishing UVR in flight can be solved either by using sun rays by means of special windows that let UVR through, or else by developing artificial sources for this purpose.

Use of spacecraft windows for the above purposes is related to the following difficulties:

> It is difficult to dispense radiation doses due to changes in bearing of the craft and, consequently, of the window in relation to the sun.

> This procedure requires development of special devices to secure the biodosimeter and body in weightlessness at a

strictly constant distance from the window and adhere to a stable orientation of the body in relation to the window.

Time for the procedures must be specially scheduled, which means the cosmonauts are not otherwise engaged.

The advantages of an artificial UVR source are stability of the spectrum and power of radiation, possibility of placing it anywhere desired in the manned compartment. UVR from an artificial source makes it possible to irradiate cosmonauts while performing various types of work.

It is known that a solid heated to over 3000°C can serve as a powerful source of UVR, which is used to produce artificial UVR sources. Use of a source with high heat during spaceflights may present some problems because of lamp overheating due to reduced removal of heat by convection in weightlessness.

Fluorescent lamps coated with a special composition--luminophores--are more suitable for this purpose. Fluorescent lamps can emit beams in a specified range, depending on the composition of luminophores.

Thus, use of UVR during spaceflights puts the following tasks to researchers:

Investigation of biological effects of UVR on man during long-term flights.

Investigation of effect of different spaceflight factors on biological effect of UVR.

Determination of preferred UVR spectrum of operator exposure during long-term spaceflights.

Experimental validation of UVR method for operators during long-term missions (mode of irradiation, duration, frequency, etc.).

Experimental validation of medical and engineering specifications for UVR sources as related to long-term missions (preferred spectrum of radiation, power).

Use of UVR during spaceflights requires solving several complex theoretical and practical problems.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

NATURE OF CIRCULATORY REGULATION IN PILOTS

[Article by V. G. Doroshev, Z. A. Kirillova and A. P. Vanarshenko]

[English abstract from source] Dynamic observations over
a group of pilots within a working week during three months
have shown that blood pressure increases to meet the re-
quirements via higher cardiac output. When stresses grow
and fatigue sets in, the pattern of circulation regulation
changes so that elevated blood pressure is maintained due
to an increased peripheral resistance. Differential approach
to the pattern of blood pressure regulation makes it possible
to assess the degree of circulation adaptation to various work
work loads.

[Text] Arterial pressure (BP) level not only indicates the state of an
individual, but is the main indicator for detecting disturbances in vascular
tonus. A change from transient elevation of BP to stable rise is associated
with changes in types of regulation [8].

The types of control of central hemodynamics can be investigated only with
use of complex tests and long-term observation of a patient in a therapeutic
and preventive institution.

Our objective here was to study circulatory regulation in healthy pilots at
work.

Methods

We screened 17 pilots 27-33 years of age, who were under observation for
3 months.

On flight days, they were examined 1 h before the flights and on ground
training days, 2 h after the start of their work day.

Using modules of the Polynome-2M apparatus [3] we recorded simultaneously,
with the subjects at relative rest, the tachooscillogram of the brachial
artery, sphygmograms of the carotid and femoral arteries. From the

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obtained curves, we determined the heart rate (HR), minimum (BP_d), mean (BP_m), lateral (BP_l) and end (BP_e) arterial pressure, as well as duration of ejection period (EP) for the left ventricle, lag time of pulse wave in the carotid artery--femoral artery segment. Using the formula of Bremser-Ranke as modified by N.N. Savitskiy [5], we calculated stroke (SI) and cardiac (CI) indexes of cardiac output, specific actual (SAR) and specific working (SWR) resistance of peripheral vessels.

The data were submitted to statistical processing with use of the parametric (Student's criterion) method. The dynamics of changes in circulatory parameters were compared to the dynamics of work load, which was assessed by the complexity of flight assignments using a specially developed method.

Results and Discussion

It was determined that there is significant variability of hemodynamic parameters of pilots on flight and preparation days (Table 1). With increase in flight load, circulatory parameters, which had a tendency toward reliable increase, became virtually the same as on the days of ground training and flight days. The increment in hemodynamic parameters was not associated with increase in range of variation. Such dynamics of changes are indicative of prevalence of influence of the sympathetic branch of the autonomic nervous system on circulation.

BP elevation was associated with reliable increase in peripheral resistance. The increase in SAR/SWR ratio was indicative of progressive peripheral vascular spasm, while the circulatory reaction as a whole was overtly hypertensive. Preservation of homeostasis in the circulatory system with virtually unchanged inotropic function of the heart (retention of cardiac output) was effected by some activation of chronotropic function (reliable increase of HR) and substantial increase in vascular tonus.

A reduction of flight load in the 3d month of observation led to relative drop of dynamic mean, lateral, systolic BP and cardiac output indicators. However, peripheral vascular resistance remained high. Such dynamics are indicative of gradual decrease in sympathetic influence on the heart with diminished flight load and (perhaps) diminished myocardial sensitivity to sympathetic factors [4].

The increase in cardiac output in the first 2 months of observation, which was associated with increase in peripheral resistance, caused BP to hold at a level consistent with the loads. This mixed type of regulation of cardiovascular function should probably be evaluated as the most favorable and optimum [2]. Thereafter, the role of cardiac output in maintaining BP diminishes, with concurrent increase in importance of peripheral resistance, which is indicative of change in function of regulatory mechanisms to the vascular type of regulation. There was no appreciable BP rise, since cardiac output was reduced.

It must be noted that, in the course of the 3-month observation period, mean dynamic BP exceeded the norm for the pilot's age group by a mean of 9-16 mm Hg, which could be evaluated as a sign of borderline hypertension,

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Table 1. Hemodynamic parameters of pilots during 3-month observation (M±m)

Month	Flight load arbitr units	Activity	HR/min	BP_d, mm Hg	BP_m, mm Hg	BP_l, mm Hg	BP_e, mm Hg	EP, s	PWPV, m/min	SI, ml/m²	CI, l/min/m²	SAR/SWR, %
1	250	Ground prep.	64±3	67±2	88±2	101±2	125±2	0.27±0.03	6.9±0.2	46±4	2.80±0.3	107±3
		Flight shift	74±2*	72±1*	98±1*	110±2*	139±2*	0.26±0.06	7.3±0.1	41±2	2.93±0.2	119±2*
		Ground prep.	67±2	88±2*	97±2*	110±2*	135±1*	0.26±0.05	7.0±0.2	43±5	2.91±0.4	118±2*
2	377	Flight shift	71±2	98±1*	101±1*	114±2*	141±2*	0.27±0.05	7.1±0.1	44±4	3.02±0.2*	124±2*
3	196	Ground prep.	72±1*	71±1*	94±1*	101±1	128±2	0.24±0.05*	7.0±0.3	34±1*	2.45±0.1*	117±1*
		Flight shift	73±3*	74±2*	98±2*	110±2*	144±2*	0.25±0.03*	6.8±0.2	42±5	2.91±0.3	121±2*

* $P<0.05$. Here and in Table 2: PWPV--pulse wave propagation velocity.

Table 2. Changes in pilots' hemodynamic parameters during work week (M±m)

Day of week	Activity	HR/min	BP_d, mm Hg	BP_m, mm Hg	BP_l, mm Hg	BP_e, mm Hg	EP, s	PWPV, m/min	SI, ml/m²	CI, l/min/m²	SAR/SWR, %
Mon	Ground prep.	71±2	66±1	91±1	106±2	132±2	0.27±0.04	7.0±0.1	45±2	3.1±0.1	112±2
	"	72±3	64±1	88±1*	104±1	131±2	0.27±0.04	6.9±0.1	45±3	3.3±0.3	108±1
Tue	Flight shift	66±3	73±1	100±2	115±2	142±2	0.27±0.05	7.1±0.1	48±2	3.2±0.1	123±2
Wed	Ground prep.	75±3	66±2	90±1	104±2	131±2	0.26±0.05	7.3±0.2	41±3	3.1±0.4	111±2
	Flight shift	71±2	75±1	99±1	113±1	142±1	0.27±0.04	7.4±0.1*	43±2	3.0±0.1	121±1
Thu	Ground prep.	70±2	67±3	91±2	106±3	132±2	0.26±0.02	7.1±0.1	45±3	3.2±0.2	112±2
	Flight shift	73±2	76±2*	100±2	117±2	144±2	0.26±0.06	7.8±0.1*	41±2	2.9±0.1*	123±2
Fri	Ground prep.	67±3	64±2	87±1*	103±2	128±3	0.27±0.05	7.2±0.2	46±3	3.0±0.3	107±2*
	Flight shift	72±1	71±1	99±1	110±2	141±2	0.26±0.06	7.3±0.5	42±3	2.8±0.1*	121±2

* $P<0.05$.

or a risk factor for essential hypertension. According to [6], three hemodynamic variants of circulatory regulation are formed according to CI level: hyperkinetic, eukinetic and hypokinetic (5.67-4.32, 4.31-2.96 and 2.95-1.59 ℓ/min/m^2, respectively). According to this classification, the dynamics of circulatory changes in the pilots throughout the observation period corresponded mainly to the hypokinetic type of hemodynamic regulation. At the present time, there are data to the effect that the hemodynamic heterogeneity of the population may be due to genetic and age-related differences, on the one hand [1, 7], and be the consequence of developed disease, on the other [8]. According to these theses (making certain assumptions), the tested pilots could be referred to the group of subjects with stable hypertension. However, the relatively low BP recorded during their professional activities made it possible to expound the hypothesis that the type of circulatory system regulation reflects the dependence between magnitude of stress factors and presence of functional reserves. This flexibility of changes in cardiac output probably causes retention of constant cardiovascular functions and resistance of the population to diverse environmental factors.

To confirm this theoretical premise, it would be expedient to consider the dynamics of circulation during the first work week (Table 2). On the days of ground training, the parameters of circulation remained at virtually the same level, which is indicative of adequate rest being scheduled for the pilots. The state of hemodynamics can be classified as the eukinetic type of regulation, judging by the nature of changes in parameters of cardiac output and peripheral vascular resistance. On the flying shift days, we observed elevation of BP, increase in tonus of great and peripheral vessels (in several instances, this progressive increment of BP parameters was statistically reliable by the end of the week). On the first two flight days (Tuesday and Wednesday), the nature of changes in hemodynamics was eukinetic, as on the ground training days, whereas on the next two flight days, it corresponded to hypokinetic type of regulation.

Typically enough, we failed to demonstrate hemodynamic states that could be referred to the hyperkinetic variant of circulatory regulation in their quantitative and qualitative parameters, either during the work week or the 3-month observation period. Healthy [7] and sick [8] subjects presented a distribution of all three types of regulation in a state of absolute rest, when the subjects were not engaged in their professional work, whereas operational calm of pilots during work is a state of recovery of functions following prior flights or mobilization of these functions for impending loads.

The obtained data warrant the assumption that the type of circulatory regulation is not a constant characteristic of this system, but a manifestation of adaptive reactions and level of functional reserves during adaptation to the nature and severity of environmental factors. Further investigations in this direction will enable us to gain deeper knowledge on this score.

Thus, constant changes in cardiac output and peripheral vascular resistance are genetically determined defense mechanisms of the circulatory system that provide for optimum BP. The range of changes in cardiac output and peripheral vascular resistance characterizes the functional reserves of the circulatory system. Differentiation between types of regulation according

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to changes in parameters of cardiac output enables us to assess the degree of adaptation of the circulatory system to existing environmental factors. The most favorable regulation of circulation is of the hyperkinetic type. The hypokinetic type of regulation is typical of intense function of the circulatory system, which increases the risk of prehypertensive states.

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PSYCHOEMOTIONAL PILOT STRESS PRIOR TO EJECTION AND ITS ROLE IN APPROPRIATE PERFORMANCE

[Article by A. P. Kozlovskiy and A. F. Kovalenko]

[English abstract from source] It was demonstrated that with respect to the psychoemotional state real and simulated catapulting events were similar. The time-course variations in the latent period of the motor reaction were obtained. The time interval between the command "Go" and the catapulting event was found to increase significantly in relation to the latent period. This was correlated with the level of psychoemotional strain.

[Text] Impending ejection from a modern aircraft presents a serious psychological problem. The pilot's awareness of the potential danger of impact head-pelvis accelerations, excess pressure, aerodynamic forces, accelerations of rotation and braking in a current of air lead to additional increase in psychoemotional tension, which arises due to development of the emergency situation, with all ensuing consequences [1]. Our objective here was to determine the psychophysiological capabilities of an individual in a state of psychoemotional stress, with regard to appropriate performance for emergency abandonment of the aircraft.

Methods

A situation model was produced by exposing subjects to the two main factors characterizing the ejection process: head-pelvis impact acceleration and air current. In some cases, we also used positive pressure (up to 1400 mm water) breathing.

The tests were conducted on an aerodynamic stand. The ejection seat (ES) with the subject was placed along guides into the region of action of current with impact accelerations of 6 to 12 G lasting up to 0.13 s.

Air current velocity constituted up to 1250 km/h and changed as a function of time according to a law that was close to real time. Total time of exposure to air current did not exceed 1 s and, at maximum current velocity, 0.3 s. In the studies we recorded such technical parameters as head-pelvis

accelerations, air current velocity and its change in time. Safety of the tests was assured by selection of appropriate parameters of impact head-pelvis accelerations as to magnitude, exposure time and build-up rate, as well as by a system of protection of subjects against the effect of the air current, which included special individual gear, a system of immobilizing them in the seat, device to limit sprawling of limbs and head movements, deflector, etc.

To assess the psychoemotional state, we recorded the electrocardiogram (ECG), arterial pressure (BP) according to Korotkov and Savitskiy, respiration rate (RR), minute respiration volume (MV), oxygen uptake (OU), heat production (HP) and results of medical interrogation.

The study of appropriate performance included determination of the following parameters: latency period of motor reaction (LPMR), precision of reproduction of 3-s intervals and specified muscular exertion, duration of interval from the command to "go" to ejection, time of appearance of first specified movement, precision of reproduction of specified rhythm of movements per minute.

A total of 21 subjects 19 to 35 years of age participated in 276 tests. They were all deemed to be fit for flight work without restrictions by a medical commission. Each was exposed to the air current for 2 to 40 times.

Results and Discussion

According to the results of a physical examination, instrument tests performed right after the investigation and observation for several days, the condition of the subjects was indicative of absence of traumatic injuries. This enabled us to assess exposure to impact head-pelvis accelerations and air current as safe with regard to trauma under concrete conditions.

We assessed the degree of psychoemotional tension according to reactions of the cardiovascular system (CVS) and respiration, as well as level of metabolic processes.

Under laboratory conditions, the heart rate (HR) of all subjects did not exceed 72-90/min 30-20 min prior to exposure to stress factors. As the time diminished, HR increased, reaching a maximum at 5-10 s prior to ejection in air current, 5-10 s after it, constituting 140-170/min, and impending exposure to head-pelvis impact accelerations and air current together had the strongest psychological influence, as reflected by the greater degree of HR changes under these conditions, as compared to impact accelerations or positive pressure breathing alone (Figure 1a).

Commands given to the subjects, which were delivered on a lighted panel, served as conditioned stimuli: "get ready," "attention," "go," as did increase in volume of sound with increase in velocity of air current. Amplification of current sound with repeated exposure was reinforced by raising its pressure on the anterior surface of the body.

Another interesting fact was that the build-up of HR was more marked and occurred sooner when the subject was warned of the increase in velocity of air current. This was indicative of increased psychoemotional tension due
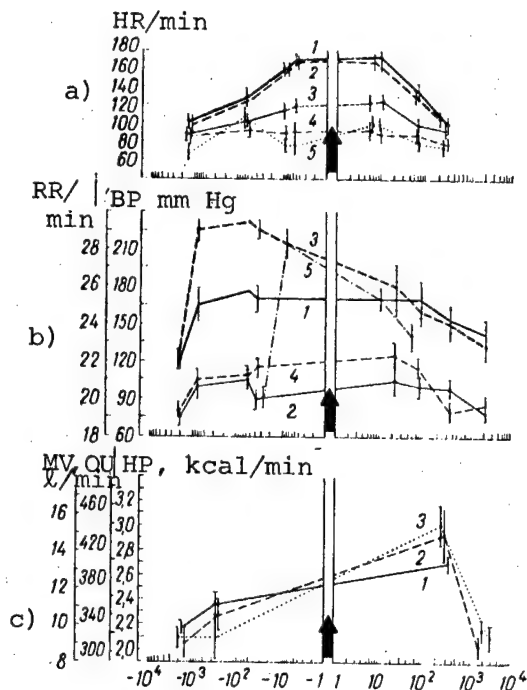
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Figure 1.
Dynamics of parameters of subjects'
condition at different times in rela-
tion to effects of ejection factors
  a) HR change (per min):
    1) ejection into air current
    2) "deferred" test
    3) ejection without exposure
       to air current
    4) positive pressure breathing
    5) ejection into air current
       with prior aminazine intake
  b) BP and RR changes:
   1,2) maximum and minimum BP with
       ejection into air current
   3,4) same with ejection into air
       current and positive
       pressure breathing
    5) RR with ejection into air
       current
  c) changes in MV (1), OU (2) and
     HP (3)
X-axis, time in relation to
exposure (s)

to second-signal stimuli, which was con-
firmed by the analogous reaction in
cases of a "deferred" test, when ex-
posure to impact accelerations and
air current was canceled at the last
minute (see Figure 1a).

The results of tests, in which the sub-
jects were given aminazine beforehand
are indicative of the conditioned reflex
nature of the observed reactions (see
Figure 1a). This agent depresses the
tonic and excitatory influence of the
reticular formation on the cerebral
cortex [3]. The insignificant changes
in HR with intake of aminazine are in-
dicative, in turn, of absence of spe-
cific effect of impact accelerations
and air current of the parameters
used with the set of protective gear
on the cardiovascular system.

The BP dynamics supplement the des-
cribed cardiovascular system findings.
BP parameters were in the range of
148 and 90 to 100 and 60 mm Hg 20-30
min prior to the test. With decrease
in time before the test, BP rose
(Figure 1b). There was particularly
marked elevation of BP in the case of
adding positive pressure breathing
(see Figure 1b). In this case, we
observed headaches and cyanosis of
the facial integument. These distinc-
tions enabled us to assess the test
results not only as reflecting psycho-
emotional tension, but effect of
positive pressure on reflexogenic
zones of the tracheobronchial system
of the lungs. An analogous assess-
ment was made of the slowing of pul-
monary circulation observed in experi-
ments on animals [2]. For this reason,
the results of tests with positive
pressure breathing were excluded from
our analysis of motor reactions.

There were typical reactions by the respiratory system. RR was in the range
of 18-24/min 30-20 min before ejection into an air current. As the time
before ejection diminished, this parameter rose (see Figure 1b). The RR
change was associated with increase in MV (see Figure 1b). There was also
increase in OU, as compared to parameters recorded under laboratory condi-
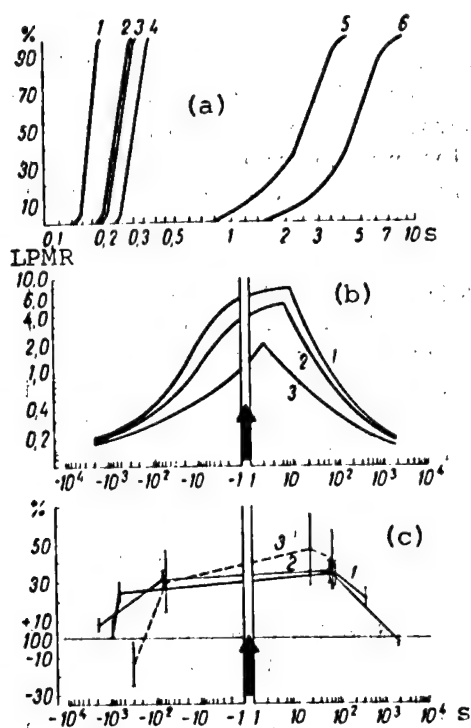tions (see Figure 1c).

Figure 2.

Changes in subjects' motor reactions at different times in relation to effects of ejection factors

a) integral functions of distribution of motor reaction parameters; x-axis, LPMR time (s); y-axis, number of cases (%)
  1) LPMR under laboratory conditions before ejection
  2,3) LPMR in ejection seat before and after ejection
  4) LPMR in ejection seat before and after sound of air current
  5) interval from "go" command to ejection
  6) interval from ejection to first motor reaction
b) curves of equally probable effects:
1-3) 95, 50 and 5% effect, respectively
Here and in (c), x-axis, time of relative exposure (s); y-axis, LPMR time (s). Arrowhead shows ejection into air current
  c) change in error (%) of reproduction of movement operations:
  1) assigned rhythm
  2) counting 3-s intervals
  3) reproduction of muscular exertions

HP level rose by 100-300 cal/min before ejection into air current, maximum increments being observed 15-20 min after the test--to 1000 cal/min (see Figure 1c).

Thus, these parameters of functional state are indicative of significant changes related to impending exposure to impact head-pelvis accelerations and air current. Combined analysis of dynamics of different parameters of the cardiovascular system, respiration, HP and hormonal reactions revealed that they are related to psychoemotional tension. Hence, appropriate performance by the subjects under these conditions may reflect distinctions that occur under actual conditions of impending emergency abandonment of an aircraft.

It was established that duration of LPMR under laboratory conditions, as well as in the ejection seat prior and after the test, differed insignificantly (Figure 2a). We observed increase in LPMR with appearance of the sound of air current (see Figure 2a).

The listed LPMR time should hypothetically correspond to the interval between the "go" command to switching on of ejection mechanism, since the subject confirmed his readiness to eject by depressing the appropriate check sensor and waiting for this command. But we failed to demonstrate such consistency in our test (see Figure 2a). Psychoemotional tension affected ejection decision making, regardless of prior readiness to participate in the test. The faster the air current, the more marked was hesitation [slowing?]. The degree of hesitation is described by the following equation:

$$y = -4.129 + 6.534 \cdot 10^{-3} x (r = +0.869; \ P < 0.01),$$

where y is time from "go" to ejection (s) and x is current velocity (km/h).

Arrowhead indicates exposure

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Data on duration of interval from "go" signal to ejection (see Figure 2a) corresponding to a 95% level are the most reliable for consideration of emergency signals as well in the features of information systems, particularly in comparison to the results of determining latency period of motor reaction under laboratory conditions and even in flight, but without an objectively existing stress state in the subjects.

The increase in interval between end of exposure to air current and first motor reaction was even more significant (see Figure 2a), which is attributable to maximum psychoemotional stress, and it could hypothetically serve as the cause of failure to eject from the aircraft in emergency situations if time is shorter than indicated in Figure 2a (curve 6) and Figure 2b, which illustrates curves of equally probable effect in accordance with logistic functions (see Table).

Coefficients of logistic function of the $y \dfrac{100}{1 + 10^{a+bx}}$ type of parameters of motor reactions

Curve from Figure 2a	Parameter examined	Time before (−) & after (+) test	Coefficients	
			a	b
1	LPMR in the laboratory	−30 min	19.733	−112.76
2	LPMR in ejection seat	−10 min	8.634	−39.243
3		+10 min	9.026	−39.243
4	LPMR with sound of air current	−1 min	15.643	−52.143
5	Time from "go" to ejection*	−−	2.305	−0.941
6	Time from end of air current to first motor reaction	−−	2.312	−0.491

*For Vi = 1000–1050 km/h.

The pilot's ability not only to react and make decisions rapidly when he is in stress, but to perform specific actions in a specific order is very important to the outcome of an emergency situation. The subject was asked to depress a contact sensor with his left hand for 10 s in a previously learned rhythm (60/min). The deviations were the most substantial in the 1st min after the test (Figure 2c), and they were unrelated to intensity of factors used.

The subjects had a distorted sense of time. For example, after the test, there was a mean 35% overestimation of 3-s periods (subjectively estimated) (see Figure 2c).

Data on change in specified muscular exertion (in arbitrary units; see Figure 2c) provided additional information indicative of the appreciable effect of psychoemotional stress on ability to perform appropriately.

Thus, this investigation established that impending ejection with exposure to impact head-pelvis accelerations similar in parameters to actual ejection and to an air current of near-sonic and supersonic velocity lead to development of marked psychoemotional stress in pilots, with typical changes

in the cardiovascular system, respiration and other systems of the body, which reach a maximum just prior to and after ejection.

The demonstrated patterns of formation of appropriate performance by subjects under conditions simulating the actual situation prior to ejection, enable us to assess a pilot's capacities and time characteristics of his performance with reference to decision making and ejecting.

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EFFECT OF INTENSIVE OPERATOR WORK ON LIPID PEROXIDATION PROCESSES IN MAN

[Article by S. M. Ivanova, O. N. Orlov, S. S. Brantova, O. I. Labetskaya,
N. A. Davydova, A. Ye. Zezerov and A. S. Ushakov]

[English abstract from source] It has been demonstrated
that the stress associated with an active mental work for
2 hours leads to a high rate of lipid peroxidation which
results in a greater amount of products of lipid peroxida-
tion in blood and pentane in exhaled air. Simultaneous
measurements of blood catecholamines have shown their sig-
nificant increase immediately after exposure to the stress
effect. It can therefore be concluded that a stress
situation enhances lipid peroxidation in the human body.

[Text] Animal studies have established that there is marked activation of
lipid peroxidation (LPO) in different organs in the presence of stress
states. Such activation and accumulation of hydroperoxides are the decid-
ing link in the pathogenetic chain of stress-caused damage, which can be
entirely prevented by preadministration of LPO inhibitors--antioxidants [3,
5, 7]. However, the question of the extent to which this thesis, which
has been validated in animal experiments, can apply to man has not yet been
answered.

At the present time, it can be considered proven that lower hydrocarbons are
formed with activation of LPO in animals and man, as a result of successive
degradation of lipid peroxides and splitting of alkoxyl radicals: methane,
ethylene, ethane, propane, butane, pentane, hexane and others [9, 12].
These gases are exhaled in air, and their levels are a specific and highly
sensitive criterion of LPO intensity.

Our objective here was to determine whether LPO activation occurs in humans
under stress caused by intensive intellectual work to be performed within
time limits.

Methods

We used the method of determination of LPO gas products in exhaled air and
LPO products in blood. We assayed plasma catecholamine levels, which
characterize the state of the adrenergic system under stress.

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For this purpose we examined 20 healthy subjects, 13 of whom were submitted to stress. The latter was produced in the form of operator work involving solution of seven rather difficult mental problems in a limited time. Total duration of the test was 2 h [2].

Gas products of LPO in exhaled air, primary and secondary LPO products and catecholamines in blood were assayed 24 h and 15 min before the stress situation, as well as 15 min and 24 h after it. We measured epinephrine and norepinephrine concentration 45 min after work, and the levels of pentane in exhaled air after 1, 2, 4 and 5 days.

In performing a quantitative analysis of hydrocarbons in exhaled air, we proceeded from the thesis that ω-6-polyunsaturated fatty acid residues of phospholipids were the predominant LPO substrate and, accordingly, pentane was the main quantitatively predominant gaseous product of LPO [11]. For this reason, to assure maximum sensitivity of the method, we assayed pentane content of exhaled air. We used polyethylene 2-ℓ packages, which were first blasted with pure nitrogen, to collect samples of exhaled air. The organic substances contained in exhaled air were concentrated in a 440 mm column filled with TENAX-C (60-80 min; Netherlands), a sorbent that traps organic substances and passes inorganic ones. Chromatographic analysis was performed on a Perkin Elmer (Sweden) gas chromatograph with flame-ionization detector. The glass columns (3 mm × 2 m) were filled with activated aluminum oxide, Aluminia F-1 (45-60 mesh; Perkin Elmer, Sweden). We used helium as the gas carrier. Helium delivery was 10 mℓ/min, hydrogen 40 mℓ/min and air 400 mℓ/min. Temperatures were 190°C for columns, 210°C for the injector and 220°C for the detector. Integration of peak areas was performed on a Perkin Elmer Computing Integrator (Sweden). Pentane appeared within 2.5-3 min. The margin of error of the method did not exceed 10%. We expressed the concentration of pentane in exhaled air in nmol/ℓ.

Lipids were isolated from blood by the method of Bligh and Dyer [8]. Primary and secondary LPO products were demonstrated by polarography [1], epinephrine and norepinephrine in blood plasma were assayed by a fluorimetric method [10].

Results and Discussion

Figure 1 illustrates typical chromatograms obtained in tests of exhaled air before and after exposure to stress [1]. The fourth peak on the left, in both figures (arrowhead), correpsonds to pentane. The figure shows that there is appreciable increase in pentane content of exhaled air after stress. Quantitative analysis revealed that pentane content in exhaled air before the stress factor constituted a mean of 1.71±0.34 nmol/ℓ, concentration of primary and secondary LPO products was 1.06±0127 nmol/mg lipids and 41.43± 6.74 nA/mg lipids, while epinephrine and norepinephrine levels were 0.49± 0.05 and 0.69±0.05 μg/ℓ, respectively. We observed elevation of catecholamine levels 15 min before starting to work (by 42% for epinephrine and 18% for norepinephrine), as well as of LPO products (by 68% for primary products and 35% for secondary) in blood (Figure 2), the pentane content of exhaled air remaining virtually unchanged. After the stress situation, there was increase in plasma epinephrine and norepinephrine content, blood LPO products and pentane content in exhaled air. It must be noted that,
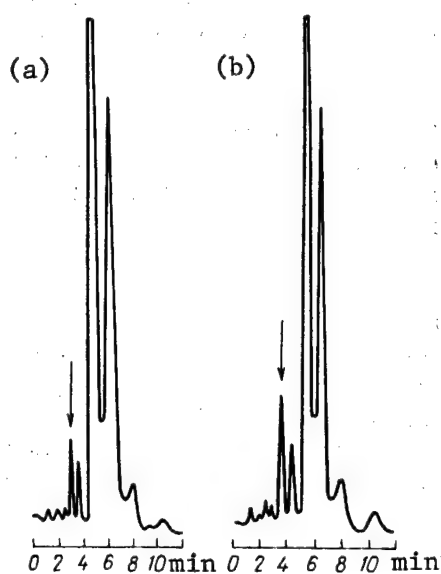
Figure 1.
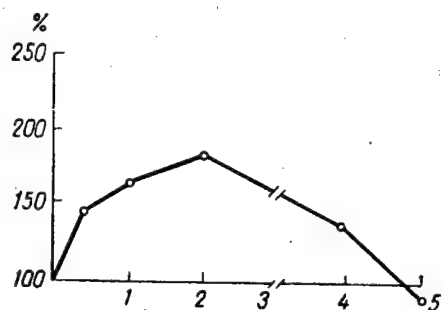Chromatograms of exhaled air before (a) and after (b) operator work

Figure 2.
Change in levels of LPO products and catecholamines in blood during experiment
I) 15 min before stress
II, III, IV) 15, 45 min and 24 h after stress
1) epinephrine
2) norepinephrine
3) primary LPO products
4) secondary LPO products

Figure 3.
Pentane content of exhaled air after experiment. X-axis, postexperiment days

although the increase in concentrations of epinephrine and norepinephrine was significant (by 190 and 75%, respectively), it was relatively brief. One day after the stress factor, catecholamine content was close to a normal level (as compared to data obtained 24 h before stress; see Figure 2).

Level of primary and secondary LPO products in blood was 174 and 56% increased, respectively, 15 min after work. The levels of these products remained high 1 day after work (78 and 44% elevation, respectively).

Pentane content of exhaled air was 33% higher 15 min after stress and 72% higher after 2 days. The concentration of this hydrocarbon reverted to the base level only by the 5th day (Figure 3).

Thus, elevation of catecholamine content, which reflects excitation of the adrenergic system that is typical of stress, precedes maximum activation of LPO, as indicated by the increase in pentane content of exhaled air and LPO products in blood. It is significant that the stress reaction of LPO activation, which plays an important part in damage to cell membranes [4], lasted
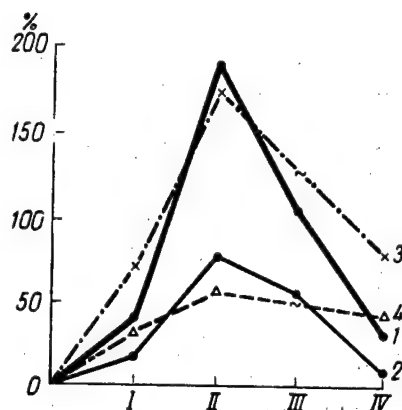
for a rather long time after stress. Its dynamics and duration coincided with dynamics and duration of LPO activation in internal organs in the presence of emotional-nociceptive stress in animals [6]. This warrants the belief that an increase in LPO gas products in exhaled air reflects the degree of LPO activation in cells of vital organs. On the whole, the results indicate that stress, in humans as in animals, which is unrelated to direct injury by exogenous factors, elicits activation of peroxidation, as manifested by increase in LPO products in both blood and exhaled air. The latter provides a real possibility of using antioxidants to protect man against stress-induced injuries, and warrants the belief that assay of LPO products in exhaled air and blood is an important criterion of intensity of stress effect and effectiveness of factors that protect man against stress-related damage.

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EFFECT OF RHYTHMIC PHOTIC INTERFERENCE ON WORKING ELECTROENCEPHALOGRAM
AND EFFICIENCY OF HUMAN MOVEMENTS

[Article by Ye. T. Petrenko and L. A. Yermukhametova]

[English abstract from source] The effect of rhythmic
light flashes on the space-time pattern of brain bio-
potentials during motor functions and biomechanical
efficiency of man's actions was investigated. As the motor
model we used the ability to maintain equilibrium when stand-
ing on the toes of one foot. Electroencephalography (EEG)
from 12 neocortical areas and oscillations of the body mass
center (stabilography) were recorded in 20 men who performed
the exercise under normal conditions and during light
flashes of 12 Hz. The resultant EEG and stabilograms were
exposed to correlations-spectral and coherent analysis with
the aid of an EC-1035 computer. Light flashes induced a
change in the EEG peaks and flicker fusion frequency, a sig-
nificant increase (by 23-108%, $P<0.05$) of the density of
biopotentials corresponding to the light stimulation frequency,
and a redistribution of the number of high intercentral cor-
relations between neocortical motor centers. When the light
flashes were presented, 75-85% test subjects showed a 0.19-
0.26 increase in the biopotential coherence of the premotor,
motor and sensomotor areas. They also exhibited a signifi-
cant decrease in the body stability ($P<0.01$) and an increase
in the stabilographic amplitude and frequency ($P<0.01$). It
is suggested that the decline of biomechanical efficiency is
associated with the disorders of the space-time integration
between neocortical centers involved in the motor control
system that are responsible for the execution of motor acts.

[Text] Noise immunity of the central nervous system is mandatory in the
work of pilots, operators and cosmonauts.

Rhythmic flashes of light are distinctive interfering factors [2, 10, 13].
It was established that they elicit changes in electrical processes of the
animal and human brain, when at rest, which are known as rhythm-change
reactions [3, 7, 11, 13-16]. It was reported that light flashes at

frequencies in the α range affect human work capacity and the spectral composition of the electroencephalogram [2, 10].

In this connection, our objective here was to test the effect of 12-Hz light flashes on time and space organization of bioelectric potentials of the brain during motor activity and biomechanical efficiency of human actions.

Methods

A total of 20 subjects 19-22 years of age participated in this study. Balancing on the toes of one leg served as the motor model. This exercise has a complicated biomechanical structure, but at the same time it is not associated with marked activity of head and neck muscles that would distort the electroencephalogram (EEG).

The subjects performed this exercise under normal conditions and in the presence of photic stimulation at a frequency of 12 Hz and intensity of 30,000 lux, generated by a photostimulator. While the subjects maintained their equilibrium, we used a Medicor electroencephalograph for simultaneous recording of the EEG from 12 regions of the neocortex and stabilograms. Bioelectric potentials of the brain were derived monopolarly from the frontal, visual, inferior parietal, sensorimotor and premotor regions, as well as from the regions of motor muscles of the arms and legs. Cup electrodes made of niobium were attached to the head with collodion.

Segments of the EEG and fluctuations of general center of gravity (GCG) of the body lasting 2-6 s at 17 ms intervals were converted into variable-sign series and inputted in an EC-1035 computer. For quantization and primary conversion of signals, we used the Elektronika-60 microcomputer. Using Foureir conversion between any pairs of recorded processes, we calculated the coefficients of paired correlation of autospectral and cross-spectral functions and coherence function.

Results and Discussion

Light flashes led to reliable (P<0.01) decrease in balance-holding time, increase in stabilogram amplitude and frequency. Thus, the subjects held their balance with delivery of photostimulation for 44% of the time under ordinary conditions, whereas the amplitude of shift of GCG of the body reached 110-220%. Photic stimulation also elicited reliable (P<0.05) increase in density of oscillations in the 6-12 Hz band in stabilogram autospectra.

The period of maintaining equilibrium in the presence of 12-Hz light flahses was characterized by marked correlation-spectral changes in the EEG. Thus, the peaks of maximum frequency spectra for the 12 EEG leads were in the range of 6-10 Hz under ordinary conditions and 11.5-12.0 Hz with photostimulation (average data for the group of 20 subjects). Analysis of individual values revealed that most coincidences of maximum peaks with frequency of flashes were observed on the EEG of the visual, lower parietal, left sensorimotor, left premotor regions, motor representation of leg and arm muscles.
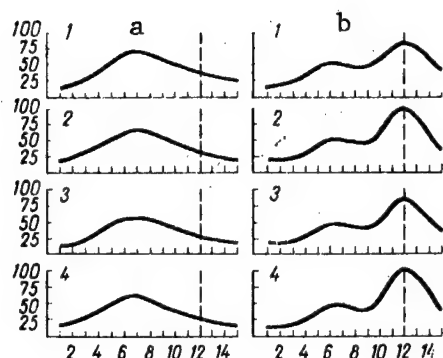
Figure 1.

Autospectrograms of left premotor region (1), motor representation of muscles of right arm (2), motor representation of muscles of right leg (3) and left sensorimotor region (4) in subject T-ko

Here and in Figure 2:

a, b) exercising under ordinary conditions and in the presence of photic interference, respectively
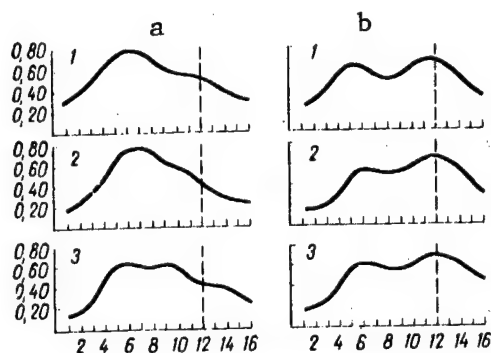
Figure 2.

Spectra of coherence of bioelectric potentials of neocortex of left premotor region and motor representation of muscles of right leg (1), left sensorimotor region and motor representation of muscles of right leg (2) and motor representation of muscles of right leg and right arm in subject Mak-v

Photic stimulation led to increase in density of peaks of frequency spectrum maximums and biopotentials, corresponding to frequency of photostimulation. Maximum growth of maximum peak density was observed in spectrograms of the optic region (by 108%), inferoparietal (67-76%), sensorimotor, left premotor, regions of motor muscles of the right leg and right arm (23-49%). These changes were observed in over 70% of the subjects. In the presence of photostimulation, the density of EEG waves corresponding to frequency of photic stimuli constituted 150-258%, as compared to ordinary conditions.

The demonstrated changes in frequency spectra were typical of premotor, sensorimotor and motor regions, left hemisphere and, in particular, left premotor region and region of motor representation of static muscles of the (right) leg (Figure 1). Thus, the density of EEG autospectral maximums for these centers of the neocortex increased by 23-25% in the presence of flashes, while bioelectric potentials at 12 Hz increased by 70-102% ($P<0.05$).

Photic stimulation elicited changes in spectrum of coherence of biopotentials in the tested EEG leads.

Under ordinary conditions, coherence function was characterized by the presence of two maximum peaks: one at a frequency of 6.3 Hz and the other, 10.2 Hz (averaged data for 30 pairs of EEG in the group of 20 people). Photostimulation led to a shift of low-frequency peak to a frequency of 5.8 Hz and decline of its value from 0.55 to 0.48. The high-frequency maximum peak shifted to 11.5 Hz, and its value rose from 0.43 to 0.57. These changes were observed in more than 80% of the subjects in most pairs of EEG (66%).

In the presence of flashes, there was increase in coherence of bioelectric potentials at a frequency of 12 Hz in premotor, motor, sensorimotor and optic regions by 0.19-0.26. Coherence of biopotentials corresponding to flash frequency in these centers of the neocortex was in the range of 0.60-0.74 (Figure 2).

There was redistribution of high intercentral correlations between the tested EEG leads in the presence of photic stimulation. Thus, under its effect there was a decrease in number of high correlations ($r>0.70$) of motor centers of the left arm (by 14%), right sensorimotor region (by 58%) and increase in motor centers of right arm muscles (by 30%) and left inferoparietal region (by 87%). There was 90% increase in number of high correlations of the frontal region with motor centers and 25% decrease in those between the left premotor region and motor representation of the left hemisphere.

Thus, rhythmic photic interference at a frequency of 12 Hz diminished in most subjects the biomechanical efficiency of complicated equilibrium and elicited on the working EEG appearance of "imposed" waves at the photo-stimulation frequency. At the same time, the flashes had no marked disruptive effect on some subjects.

Significant correlation-spectral changes in bioelectric potentials were observed in both posterior and central parts of the neocortex (premotor, motor, sensorimotor regions) functionally responsible for execution of different types of human and animal motor acts [1, 6, 8, 9, 12]. In particular, they were marked in the premotor regions which, according to clinical data, are involved in rhythmic organization of movements [9], as well as in the motor centers of the working leg, which implement the dynamic structure of complex equilibrium [1, 8, 9].

At the same time, it is known that time and space organization of bioelectric potentials of the brain is the principal mechanism of functional interaction of nerve centers [4-6, 8, 12]. Light flashes disrupted processes of time and space integration of cortical branches of the system of control of movement. This is indicated by the changes in frequency-phase relations between nerve centers of the functional system of the neocortex involved in preserving stability on a small supporting surface. The increase in amplitude of shifts of the body's GCG and density of their high-frequency spectrum, decreased stability in the presence of rhythmic photic interference are indicative of disorders in processes of controlling complex equilibrium. Apparently, distortion of optimum time and space correlations between bioelectric potentials of motor centers of the supporting leg and left premotor region leads to impairment of time structure of GCG correction within the limits of a small supporting surface.

Thus, rhythmic 12-Hz flashes diminish biomechanical efficiency of human movements due to disturbances in the system of movement control. In particular, there are changes in optimum time and space correlations between neocortical centers functionally responsible for execution of motor acts.

At the same time, analysis of individual EEG and biomechanical characteristics indicates that there is individual tolerance to photic stimulation.

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DISTINCTIONS IN HUMORAL CONTROL OF METABOLISM WITH SIMULATION OF SPACEFLIGHT FACTORS

[Article by S. Kalandarov, V. P. Bychkov, I. D. Frenkel and G. I. Proskurova]

[English abstract from source] Hormonal regulation of metabolism was investigated in test subjects of three age groups: group 1 included test subjects of 41-50 years old, group 2 test subjects of 50-57 years old, and group 3 test subjects of 26-33 years old. Test subjects from groups 1 and 2 were exposed to head down tilt (-8°) as well as linear acceleration of 3 Gz for 1 min and exercises of 450-1050 kgm before and after the tilt test. Group 3 test subjects were exposed to neuroemotional stress before, during and after the head-down test. Exposure to head-down tilt, acceleration and exercises caused adaptive changes in humoral regulation of metabolism in the test subjects of groups 1 and 2. Food supplements given to group 3 test subjects produced a normalizing effect on humoral regulation of metabolism.

[Text] There are few works dealing with the effect of hypokinesia on humoral regulation of metabolism. Some authors [11, 12] observed a decrease in function of the medullar (in rabbits) and cortical (in humans) layers of the adrenals. Others [5, 8] observed increased tonus of the adrenal element of the sympathoadrenal system (SAS) and adrenal cortex. Different findings were also made with regard to activity of energy-supplying enzymes [1, 2, 6, 13].

Some authors [3-4, 15] believe that changes due to weightlessness and hypokinesia are based on mechanisms such as altered conditions of motor activity, decline of hydrostatic pressure of column of blood on the vascular walls, changes in activity of afferent systems. The aggregate of such primary effects of weightlessness is what causes changes in fluid-electrolyte, hormonal and energy metabolisms, as well as in a number of other systems and organs. The concomitant changes in neurohumoral regulation via enzymatic systems lead to certain changes in metabolic processes [14].

We found no information in the literature containing humoral regulation of metabolism in individuals of different ages under conditions of prolonged antiorthostatic (-8°) [head-down tilt] hypokinesia (AOH) and under the combined effect of this factor with accelerations, exercise and neuroemotional stress. We submit here the results of investigation of humoral regulation of metabolism in subjects referable to 3 age groups submitted to AOH (-8°), linear accelerations and graded exercise.

Methods

The studies were conducted with the participation of 27 individuals in 3 age groups: the 1st group consisted of subjects 41-50 years of age (10 people), the 2d--50-57 years (11 people) and the 3d, 26-33 years old (6 people).

During the period preceding AOH, as well as after it, the first 2 groups of subjects were exposed to 3 Gz accelerations for 1 min and physical loads of 450, 600, 750, 900 and 1050 kg-m (3 min at each level). The third group of subjects was submitted to neuroemotional stress before (twice), during (3 times) and after (once) AOH. Stress was produced by means of a psychological test (performance of tasks varying in difficulty with a time limit).

We assessed the functional state of the SAS according to catecholamine excretion, which was assayed fluorometrically by the method in [9]. To assess adrenocortical function, we assayed 17-hydroxicorticosteroids (17-HCS) in 24-h urine [16, 17] and 11-hydroxycorticosteroids (11-HCS) in blood plasma [10]. We assessed intensity of metabolism according to enzyme activity-- lactate dehydrogenase (LDH), alanine and aspartate aminotransferases (ALT, AST) and creatine kinase (CK)--as well as levels of free fatty acids (FFA) in blood serum [7]. The values of biochemical parameters demonstrated in healthy individuals under ordinary living conditions were taken as the norm.

The subjects received a daily food allowance with energy value of 3000 kcal, which was balanced in levels of basic nutrients. To enhance adaptability, we supplemented the diet for the third group of subjects with nutrients: glucose, phosphatide concentrate, vitamins and minerals.

Results and Discussion

At all stages of the study (Table 1), the first 2 groups of subjects presented higher (P<0.002) than normal excretion of epinephrine (E) and norepineprine (NE) in urine (normal 16.9±3.8 and 65.6±5.3 nmol/day, respectively). At the indicated times, urine 17-HCS concentration increased (P<0.001), as compared to normal, which is 10.7±0.8 μmol/day.

At the same time, we found significant (P<0.01) increase in plasma 11-HCS in the 1st and 2d groups, to 772.8±30.6 and 884.0±38.9 nmol/ℓ, respectively (normal is 361.4±30.6 nmol/ℓ).

After exposure to linear accelerations, the 1st group of subjects showed an increase in AST concentration to 1783.7±140.7 (P<0.01), versus the normal value of 971.9±83.4 nmol/ℓ.

Table 1. Catecholamine (nmol) and 17-HCS (µmol) levels in 24-h urine (M±m)

Group	Parameter	Before AOH		AOH	After AOH	
		accelerat.	exercise		accelerat.	exercise
1	E	38,2±2,2	44,2±7,6	38,2±3,3	42,0±2,7	38,2±2,7
	NE	105,2±12,4	115,8±11,8	126,5±15,4	115,8±7,1	118,8±15,4
	DA	1897,6±123,4	2558,5±120,8	2036,7±233,8	2035,4±120,2	2230,6±122,8
	Dopa	102,4±8,6	134,9±13,2	113,6±20,2	124,2±16,2	129,3±7,5
	17-HCS	37,8±8,3	26,8±2,5	25,9±4,0	42,5±7,5	33,4±2,5
2	E	41,0±3,3	43,7±2,8	45,9±3,5	34,9±3,3	36,6±3,5
	NE	112,9±16,8	120,6±11,2	134,2±7,7	111,7±11,5	107,0±7,8
	DA	2536,9±264,5	2771,3±225,9	2506,2±109,1	2140,5±203,1	2234,6±217,4
	Dopa	154,6±20,8	155,6±19,8	158,7±8,6	142,5±14,7	131,8±19,8
	17-HCS	39,7±7,9	50,8±2,7	38,9±4,7	31,2±2,5	24,8±2,8

Note: Here and in Table 3, DA is dopamine.

Table 2. Enzyme levels (nmol/ℓ) in blood serum of 1st and 2d groups of subjects (M±m)

Group	Enzyme	Before AOH		AOH	After AOH	
		accelerat.	exercise		accelerat.	exercise
1	LDH	3394,0±140,95	3410,7±172,4	3487,4±270,55	4979,3±228,0	3294,0±370,1
	AST	1783,7±140,7	1408,6±110,0	1658,7±140,0	1632,0±233,4	1708,7±250,1
	ALT	2847,2±515,1	2458,8±280,1	2880,6±471,8	3450,7±661,8	2778,9±280,0
	CK	358,4±5,83	423,4±17,3	303,4±16,67	318,4±19,84	348,4±20,3
2	LDH	2593,8±210,0	2795,6±381,7	2513,8±358,4	2540,5±471,8	2890,6±591,8
	AST	1036,9±181,7	1006,9±131,7	943,5±290,1	911,8±146,7	996,9±210,0
	ALT	1648,7±388,4	1787,0±435,1	1740,3±563,4	1987,1±440,1	2563,8±486,8
	CK	576,8±110,0	541,8±61,7	721,8±148,4	971,9±300,1	1341,9±506,8

ALT concentration was somewhat high throughout the period of investigations. In the 2d group, the level of this enzyme rose reliably (to 2563.8±486.8 nmol, versus the norm of 1205.2±141.7 nmol/ℓ) during the period of graded exercise (P<0.01). CK content decreased somewhat, while LDH did not change (Table 2).

FFA concentration increased during exposure to the tested factors in subjects of the first two groups. The most marked changes occurred with graded physical exercise (0.8±0.1, P<0.02 and 1.0±0.1, P<0.01 in the 1st and 2d groups of subjects, respectively, versus the normal 0.4±0.1 mmol/ℓ).

In the 3d group of subjects, who received a food supplement, exposure to psychological stress was not associated with change in concentration of catecholamines or 17-HCS in 24-h urine (Table 3). However, the 11-HCS level rose on the 10th and 14th days (to 886.8±92.6 and 975.8±107.3, 1125.9±74.8 and 1078.6±130.7 nmol/ℓ, respectively, before and after exposure to stress, the normal being 628.3±87.6 nmol/ℓ). There were brief changes in levels of different serum enzymes. For example, during the period of anticipation of

Table 3. Catecholamine (nmol) and 17-HCS (μmol) levels in 24-h urine (M±m)

Para-meter	Before AOH				AOH stress				After AOH			
	before	after	before	after	before	after	before	after	before	after	before	after
E	29,5±4,8	34,4±2,2	30,0±3,0	36,6±3,7	27,3±3,0	32,8±4,0	37,1±3,8	27,3±4,6	25,1±4,9	33,3±6,1	30,0±4,9	28,9±7,2
NE	99,3±20,9	56,7±3,7	47,9±2,7	59,1±0,1	70,9±6,6	90,4±20,2	100,5±14,7	83,3±15,1	95,7±14,6	65,7±7,3	98,1±23,9	69,1±6,0
DA	1556,8±100,7	1972,7±198,2	1752,0±147,6	2117,7±251,7	1511,0±201,5	1782,0±246,5	2065±243,0	1815,3±211,5	1683,4±216,3	2062,8±238,9	1988,4±209,0	2056,3±214,8
Dopa	169,7±24,5	140,4±15,3	113,1±5,9	142,5±12,2	110,5±10,5	132,3±17,7	152,1±16,2	119,6±7,1	112,0±9,6	122,2±10,4	135,4±11,2	114,1±17,1
17-HCS	18,8±1,0	19,0±1,1	19,9±1,2	22,6±1,7	22,6±2,5	26,8±3,1	30,4±1,4	35,9±6,1	33,9±7,0	29,5±9,6	29,5±3,2	36,2±4,9

the stress factor before and after AOH increased to 2683.9±266.7 and 2683.9±643.5 nmol/ℓ, respectively, the normal being 1515.3±100 nmol/ℓ. In the recovery period, there was increase in AST to 500.1±56.7 nmol/ℓ ($P < 0.05$) versus the normal 363.4±35.0 nmol/ℓ, and in CK, to 2617.2±688.5 nmol/ℓ ($P < 0.02$) versus the normal 806.8±141.9 nmol/ℓ. During AOH, ALT concentration decreased to 341.7±30.0 nmol/ℓ (versus the normal 408.4±42.5 nmol/ℓ), while FFA content increased ($P < 0.05$) to 0.49±0.05 mmol/ℓ (versus the normal 0.29±0.02 mmol/ℓ).

The findings indicate that changes occurred in humoral control of metabolism aimed at its adaptation to new functioning conditions under the effect of AOH, accelerations and exericse load. The severity of this reaction was the same in the first and second groups of subjects. In the third group, we failed to demonstrate noticeable changes in the parameters tested, which could be related to the use of supplemental nutrients. Apparently, it is desirable to conduct further investigations in order to determine whether it is possible to enhance adaptability of the body in stress situations by means of alimentary factors.

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SOME HUMAN REACTIONS DURING SEVEN-DAY ANTIORTHOSTATIC HYPOKINESIA

[Article by B. F. Asyamolov, V. S. Panchenko, V. A. Karpusheva, R. A.
Bondarenko, O. A. Vorobyev, V. V. Zaritskiy, V. P. Stupnitskiy, I. G. Popov,
P. A. Lozinskiy and S. M. Ledovskoy]

[English abstract from source] Time-course variations in
the cardiovascular parameters, vestibulo-autonomic stability,
work capacity and nutritional status were measured in 20 male
test subjects, aged 19-22, who were exposed for 7 days to head-
down tilt (-10°). Beginning with days 3 or 4, new hemodynamic
ratios developed that indicated a new level of circulation
regulation and adaptation to head-down tilt. It appears that
blood redistribution towards the head led to an enhanced vesti-
bulo-autonomic stability. Renal excretion of nitrogen increased,
reaching the highest level on days 6-7. The investigations allow
the conclusion that 7-day head-down tilt may cause changes in
almost every physiological system.

[Text] There are many works dealing with the adverse effects of real or
simulated weightlessness on man [5, 9, 11, 12, 14]. At the same time, the
acute period of adaptation to weightlessness has been little-studied.
Information about changes in the body at this time (3d-7th day of adaptation)
is sometimes contradictory. For example, D. G. Maksimov and M. V. Domracheva
report a 9% decrease in pulse rate (PR) at the start of antiorthostatic hypo-
kinesia (AOH), 127% increase in stroke volume of the heart (SV) in the 1st
week of AOH and 114% increase in circulation volume (CV) [8]. According to
L. I. Kakurin [4], SV decreased to 22 mℓ on the 2d-3d day of hypokinesia and
increased somewhat by the 8th day. Systolic arterial pressure (BP_s) dropped
insignificantly on the 1st day, remaining lower than the baseline for the
next 20 days of hypokinesia. Diastolic BP (BP_d) dropped on the first 2-3 days,
then returned to the baseline [4]. Some authors have reported a decrease
in volume of circulating plasma (CPV) and a corresponding decrease in
circulating blood volume on the 1st day of simulated weightlessness [16, 18],
and others reported analogous changes on the first 3-14 days [19].

We tried to trace the dynamics of different functions of the cardiovascular
system, parameters performance on different psychophysiological levels,

to assess vestibulovegetative stability (VVS), psychological state in the course of 7 days, and to offer a physiological and hygienic evaluation of dynamics of alimentary status and two diets (24-h isocaloric allowances consisting of ordinary dishes prepared from fresh products, as well as dishes consisting mainly of canned goods).

Methods

A total of 20 male subjects, 19-22 years of age, participated in our studies; they were submitted to AOH (angle of -10°) for 7 days. Hemodynamic status was examined on the 2d and 3d days in the morning (1000-1100 hours) and evening (1600-1800 h), and in the evening (1600-1800 h) of the 1st, 5th and 7th days. BP was measured according to Korotkov daily, in the morning, right after waking up and in the evening, before going to sleep. Using an RPG-2-02 instrument, we recorded SV according to Kubicek and rheoencephalograms in the bitemporal lead. The ECG was taken using the Nehb leads and recorded on a Mingograph-81 insturment. Calibrometry and direct ophthalmoscopy (Footnote) (M. G. Kozyrkova performed these tests) were used to examine retinal vessels, the condition of which reflects, to some extent, the state of cerebral circulation [7]. As the baseline, we took the condition of retinal vessels after the subjects had spent 30-40 min in horizontal position prior to the experiments.

VVS was tested in antiorthostatic position before and on the 2d and 5th days of hypodynamia. We used the test with Coriolis accelerations: with rotation at an angular velocity of 120°/s about the vertical axis, the subjects made active up and down head movements in the vertical plane, in relation to the body's longitudinal axis. The full cycle of head movements was performed in 4 s. Resistance to motion sickness was determined according to tolerance to the test from its beginning to appearance of vestibulovegetative signs or, if none appeared, for 20 min.

Reproductive thinking was tested by the method of "finding numbers with distractions," productive perception was tested using Rorschach tables, productive and heuristic thinking was tested using the thematic apperception test and projective-associative logic test. Mental status was examined by a standardized method of personality testing. Individual psychological and personality traits were examined using a 3- and 16-factor questionnaire, the Lumer color test and others.

We examined nitrogen metabolism, excretion in urine of K and Na in order to make a physiological-hygienic evaluation of diet and dynamics of alimentary status. Using the Technicon auto-analyzer, we assayed blood levels of total protein, albumin, globulins, chlorides, glucose, K, Na, total lipids, β-lipoproteins, cholesterol, triglycerides, alkaline phosphatase and several other parameters.

Results and Discussion

A change in the subjects' position from horizontal to antiorthostatic was associated with change in subjective sensations, appearance and objective indicators. All of the subjects reported the sensation of bulging neck,

and heavy head (in occiput and temples), pulsation in cervical vessels, pressure on eyeballs, congested nose, occasionally hoarseness and headaches. There was some puffiness of the face and neck, cyanosis of mucous membranes and skin of the face. As the time of AOH progressed, their well-being improved and unpleasant subjective sensations disappeared. There was less puffiness of the face and neck.
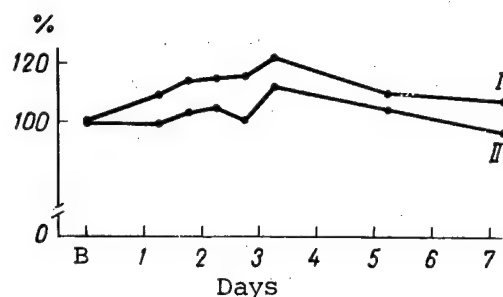

Figure 1.
Dynamics of averaged SV (I, in min) and CV (II, ms) during 7-day AOH (% of baseline--B)
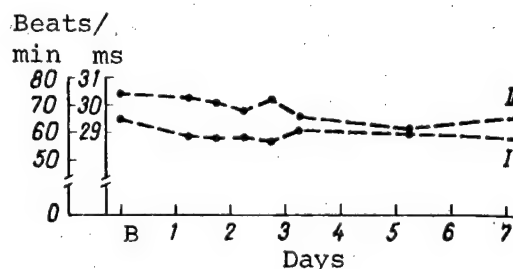
Figure 2.
Dynamics of averaged PR (I) and duration of ejection period from left ventricle (II) during 7-day AOH

Here and in Figure 2: x-axis, days of AOH.

As early as 6 h after start of hypokinesia, we observed noticeable changes in hemodynamic parameters (Figures 1 and 2). Thus PR decreased by 9%, period of ejection from the left ventricle diminished somewhat (up to the 5th day), SV increased noticeably, while CV decreased by only 100 mℓ. The changes in PR and SV differed with statistical reliability from baseline data. The parameter of pulsed delivery of blood to the head (PDBH) rose to 109.9%, while tonus of cerebral arteries of medium and small caliber (S/A) increased to 135.2%. PR continued to decline on the 2d and 3d days. Starting on the 4th day, this parameter rose somewhat, but remained below baseline values to the end of AOH ($P<0.05$). PDBH diminished on the 2d and 3d days, but from the 4th day on remained unchanged, slightly exceeding the baseline (104.8%). S/A reached its maximum value on the 3d day (183.3%), after which it gradually declined constituting 121.6% by the end of AOH. SV also rose to the end of the 3d day, but then diminished to minimal values by the end of the experiment ($P<0.05$). CV fluctuated in the baseline range throughout the experiment (changes were statistically unreliable). The dynamics of BP are submitted in Table 1. BP_s, measured in the morning, was somewhat below base values up to the 5th day of AOH, and from the 6th day began to exceed somewhat the baseline level (changes statistically unreliable). In the evening of the first 2 days, BP_s exceeded somewhat the base level, and from the 3d day on rose even more and held at this level to the end of the experiment. BP_d exceeded the baseline from the 1st day of AOH. We failed to demonstrate clearcut differences between its morning and evening values. Lowest pulsed BP (BP_p) in the evening was noted only on the 1st day (6.4% reduction). On subsequent days, it rose somewhat, remaining below base values (differences were statistically unreliable). In the morning, the BP_p decline was more marked than in the evening. Minimal values were demonstrated on the 4th day of AOH ($P<0.05$), but thereafter we observed relative recovery, although it never reached base values to the end of the experiment.

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Table 1. Dynamics of BP (in mm Hg) during 7-day AOH (M±m)

Para-meter	Base-line	Day 1 pm	Day 1 am	Day 2 pm	Day 2 am	Day 3 pm	Day 3 am	Day 4 pm	Day 4 am	Day 5 pm	Day 5 am	Day 6 pm	Day 6 am	Day 7 pm	Day 7 am
BP_s	111.1 ±1.2	113.8 ±1.7	108.3 ±0.9	114.3 ±1.6	108.9 ±1.5	118.2 ±1.7	108.2 ±1.5	115.4 ±1.5	109.4 ±1.4	116.8 ±1.5	112.3 ±1.5	117.4 ±1.9	113.4 ±1.7	115.1 ±1.3	114.1 ±1.6
BP_d	62.6 ± 1.1	68.4 ± 1.8	65.8 ± 1.7	68.0 ± 1.7	68.3 ± 1.8	70.8 ± 1.6	70.5 ± 1.9	68.8 ± 1.0	69.4 ± 1.3	66.4 ± 1.1	68.8 ± 1.3	70.2 ± 1.5	68.8 ± 1.1	67.6 ± 1.5	68.6 ± 1.8
BP_p	48.5 ± 1.1	45.4 ± 1.8	42.5 ± 1.3	46.3 ± 1.7	40.6 ± 1.6	47.4 ± 1.6	37.7 ± 1.7	46.6 ± 1.3	40.0 ± 1.4	50.4 ± 1.3	43.5 ± 1.4	47.4 ± 1.7	44.6 ± 1.4	47.5 ± 1.4	56.8 ± 1.7

Table 2.
Changes in caliber of veins and arteries (% of baseline) and correlation during AOH

Parameter	Base-line	Day 1	Day 2	Day 3	Day 4	Day 5
Arteries (A)	100	95.3	93.5	99.2	103.5	101.5
Veins (V)	100	99.5	97.0	108.2	100.5	108.0
V/A	1.111	1.163	1.185	1.195	1.105	1.175

Direct ophthalmoscopy failed to demonstrate any changes in the fundus. Calibrometry revealed insignificant constriction of arteries and veins in most cases on the 1st and 2d days of AOH, and this applied to arteries more than veins. Starting on the 3d day, we observed a tendency toward increase in caliber of retinal vessels, and it exceeded baseline values by the 5th day (Table 2). The results of these tests indicate that arterial tonus increased on the first days of AOH in the presence of virtually unchanged tonus of retinal veins. By the 5th day, there was relative decrease in tonus of veins and arteries, which could be due to development of stasis in cerebral vessels.

Analogous changes were also noted in the rheoencephalographic studies. For the first 2 experimental days, tonus of cerebral vessels increased, which we can relate to excessive influx of blood to the head, after which there was development of new hemodynamic relations indicative of appearance of signs of the body's adaptation to AOH.

In assessing the dynamics of nutritional status, we found progressive increase in nitrogen excretion in urine. This was the most distinct on the 6th-7th days and attributable to gradual development of negative nitrogen balance due to prevalence of catabolic processes in protein structures of muscle cells during limited motor activity. This was also indicated by the substantial increase in K excretion on the 7th day. Biochemical blood tests failed to demonstrate appreciable differences either in comparison to baseline period or between groups with two types of diet.

Restriction of motor activity definitely affects mental functions and results of human performance [6, 10]. Our data indicate that activity referable to reproductive thinking worsened insignificantly toward the end of the experiment, whereas productive perception, productive and heuristic thinking function changed appreciably in the direction of 10-40% worsening of results of activity. The mental status also underwent changes: increased irritability, diminished affect and activity, as a result of which results of activity are impaired.

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Thus, 7-day AOH elicits makred changes in characteristics of performance on different levels of psychophysiological content and affects man's mental status.

There are many works dealing with the role of the vestibular analyzer in onset of autonomic and other disorders associated with the space form of motion sickness [3, 13, 16 and others]. One of the most popular views of onset of space sickness is the hypothesis of sensory conflict. At the same time, the role of redistribution of body fluids is not ruled out [2, 16]. The results of testing VVS in the acute period of adaptation revealed that test endurance time on the 5th day (9.5±1.3 min) was reliably longer (according to U criterion) than in the baseline period (7.0±2.1 min), while the value of this parameter on the 2d day of hypokinesia did not differ with statistical reliability from baseline data. This indicates that VVS is subject to changes during AOH, and it depends on the time spent in this position. It can be assumed that stabilization of adaptive processes was not completed by the 2d day, but apparently by the 5th day this process was completed.

Thus, as the human body adjusts to redistribution of body fluids to the upper half of the body there is a tendency toward increase of VVS. Analysis of physiological reactions of man in the 1st week of AOH indicates that there is development of adaptive processes directed toward normalization of functions of physiological systems on a new homeostatic level. Redistribution of blood to the upper half of the body stimulates receptors of the sinocarotid region, as a result of which SV increases and PR decreases. Increased loss of body fluids was noted in the first 18 h of simulated weightlessness as a result of appearance of the Henry-Gauer reflex. Mean 24-h diuresis constituted 1256-1554 mm [1, 15]. After the 3d day, there is no longer excretion of relatively excessive amounts of fluid. CPV decreases by 481 mm [17].

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COLLAGEN, LIPID AND GLYCOGEN CONTENT OF RAT SKELETAL MUSCLES IN RECOVERY
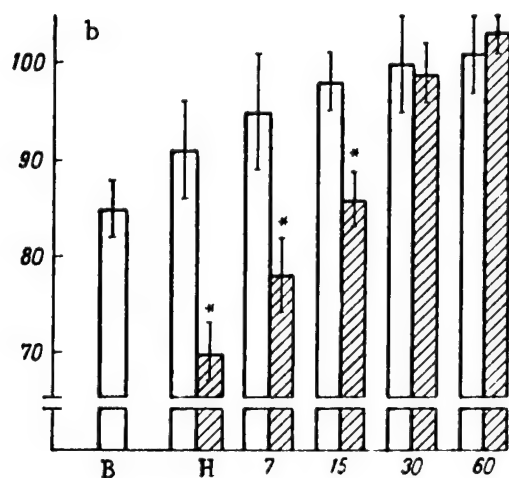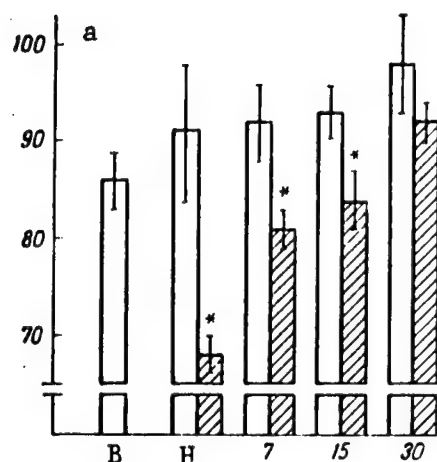PERIOD AFTER 15- AND 30-DAY HYPOKINESIA

[Article by P. P. Potapov]

[English abstract from source] On the 15th hypokinetic day
carcass mass, glycogen and lipid content in skeletal muscles
decreased while collagen content increased. The content of
collagen returned to the norm by the 7th day of the recovery
period. By that time the glycogen content increased signifi-
cantly and a week later decreased noticeably. The content of
total lipids and triglycerides was higher than the baseline
level on the 15th and 30th days of the recovery period. On
hypokinesia day 30 carcass mass and glycogen content decreased
while collagen content increased. After 30-day hypokinesia
glycogen was significantly increased on the 7th day and returned
to the norm by the 60th day of the recovery period. Lipid content
was elevated only on the 7th day of the recovery period, collagen
content returned to the norm on the 15th day of the recovery
period. Following 15- and 30-day hypokinesia carcass mass re-
turned to the baseline level by the 30th day of the recovery
period.

[Text] Strict restriction of motor activity causes serious metabolic dis-
turbances in muscle tissue [5]. Analysis of available data warrants the
assumption that metabolic changes in the recovery period are rather complex
and persist for a long time [3, 6]. This is confirmed by the results of
investigations of metabolism following rather brief (7-day) hypokinesia
[7]. Our objective here was to investigate collagen, lipid and glycogen
content of rat skeletal muscles at different stages of the recovery period
following 15- and 30-day hypokinesia.

Methods

Experiments were performed on 111 albino rats (55 served as the control) with
initial weight of 165-195 g. The animals movements were restricted by placing
them in individual small cages made of plexiglass. In the first series of
experiments, hypokinesia lasted 15 days and in the second, 30 days. Upon
termination of the hypokinetic period, the rats were transferred to common

Changes in rat carcass weight (g) in recovery period following hypokinesia

a, b) 15- and 30-day hypokinesia, respectively
B) baseline
H) hypokinesia
Arabic numerals refer to days of recovery period
White bars--intact animals, striped--experimental animals
*--P<0.05

cages. They were kept on a proper diet with water ad lib. The 1st group of rats was examined on the 7th, 15th and 30th days of the recovery period and the 2d group, on the 7th, 15th 30th and 50th days. After decapitation, we took tissue from skeletal muscles of the posterior group of femoral muscles without tendons, nerves or fascia. Isolation and quantitative assay of glycogen (GG) were performed according to the recommendations of Good et al. and Kemp and Kits [8, 9]. Total lipids (TL) were assayed by the method of Bragdon [1], triglycerides (TG) by the method of Stolz et al. [10]. We determined hydroxyproline (HP) content in hydrolysates of dry, defatted tissue [2], which enabled us to assess the amount of collagen in the muscle. We also weighed the animal's carcass.

Results and Discussion

The Figure illustrates the dynamics of change in carcass weight during the experiment. Weight loss, as compared to the control, constituted 25 and 23% on the 15th and 30th days of hypokinesia, respectively (P<0.02). After 15-day restriction of movement, carcass weight increased somewhat faster in 1 week than after 30-day hypokinesia. On the 7th day of the recovery period, weight drop of carcass constituted 12% in the 1st group of animals and 18% in the second group (as compared to control; P<0.05). Starting on the 15th day of recovery, the opposite findings were made. By the 30th day of the recovery period, this parameter came close to baseline values in both groups of animals, and there was still a tendency toward its decline in the 1st group. Thus, in spite of the difference in duration of hypokinesia, normalization of carcass weight occurred in both groups 1 month after returning to normal conditions.

The amount of collagen (according to hydroxyproline) in skeletal muscles was 30 and 32% greater on the 15th and 30th days of hypokinesia, respectively (P<0.01). This parameter came close to normal on the 7th day in the 1st group, whereas complete normalization in the 2d group occurred on the 15th day of the recovery period (Tables 1 and 2)

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Table 1. HP, TL, GG and TG content of rat skeletal muscles in recovery period following 15-day hypokinesia (M±m)

Parameter	Control	Hypokinesia (15 days)	Recovery period, days		
			7	15	30
HP, μmol/g	20,1±1,0 (8)	26,1±0,9 (6)*	21,5±1,1 (6)	20,9±1,3 (5)	20,2±1,0 (5)
TL, g%	3,04±0,09 (10)	2,56±0,11 (6)*	3,13±0,09 (6)	3,43±0,09 (5)*	3,73±0,17 (5)*
TG, μmol/g	11,9±0,3 (10)	9,8±6 (6)*	13,0±0,7 (6)	14,5±0,9 (5)*	15,4±0,6 (5)*
GG, mg%	407±21 (12)	308±36 (6)*	495±30 (7)*	274±31 (7)*	462±38 (6)

Note: Here and in Table 2, number of animals in group indicated in parentheses. Asterisk--P<0.05.

Table 2. HP, TL, GG and TG in rat skeletal muscles in recovery period following 30-day hypokinesia (M±m)

Parameter	Control	Hypokin. (30 days)	Recovery period, days			
			7	15	30	60
HP, μmol/g	20,9±0,6 (10)	27,6±1,5(5)*	24,0±1,2(5)*	20,3±0,6(5)	20,4±0,8(5)	20,6±0,8(5)
TL, g%	3,05±0,09 (12)	3,30±0,13(5)	3,36±0,09(5)*	3,03±0,14(5)	3,00±0,08(5)	3,21±0,13(6)
TG, μmol/g	12,8±0,3 (12)	13,5±0,4(5)	15,1±0,7(5)*	12,9±0,8(5)	12,2±0,6(5)	14,2±0,8(6)
GG, mg%	456±23 (23)	250±33(5)*	1006±102(6)*	883±94(6)*	592±49(7)*	489±51(6)

There are grounds to assume that synthesis of collagen does not increase appreciably during hypokinesia lasting 15-60 days, and that the changes in muscle levels of collagen are attributable more to decrease in functionally active muscle proteins than increase in absolute collagen content [4, 6]. For this reason, there is relatively smooth normalization of collagen content in the recovery period (scaled to tissue weight unit) as the amount of functionally active proteins and weight of muscle tissue increase.

GG content of muscles was 24 and 45% lower than in the control (P<0.01) on the 15th and 30th days of hypokinesia, respectively. There was dramatic elevation of this parameter on the 7th day of the recovery period, particularly in animals of the 2d group. Thereafter, their GG level gradually declined and was close to normal by the 60th day of the recovery period. In the 1st group of rats, this parameter dropped noticeably on the 15th day of the recovery period, whereas by the 30th day it had a tendency toward rise.

TL and TG content was below normal on the 15th day of hypokinesia, gradually increasing in the recovery period, so that both were above the baseline on the 15th and 30th days. TL and TG levels in muscles were close to the control on the 30th day of hypokinesia. These parameters rose somewhat on the 7th day of the recovery period and were normal by the 15th day.

Apparently there was considerable prevalence of anabolic processes by the end of the 1st week of the recovery period. An increase in protein synthesis was found, in particular, in muscles [6]. On the 7th-10th days after 7-day hypokinesia there was accumulation of GG in the liver and skeletal muscles [7]. The demonstrated increase in supply of this polysaccharide

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was apparently also attributable to its increased synthesis. In the recovery period, processes of lipid synthesis apparently also prevailed over their degradation. However, after 30-day hypokinesia, there was less marked excessive accumulation of TG in skeletal muscles and it disappeared faster. In the recovery period following briefer hypokinesia, the changes are shifted to later stages and they are more stable.

The considerable fluctuations of GG levels and accumulation of TG in muscles in the recovery period after 15-day hypokinesia can apparently be interpreted as an unfavorable phenomenon. These changes are indicative of impaired balance between synthesis and utilization of carbohydrates and lipids in the recovery period. Recovery of metabolism in muscle tissue was even smoother after 30-day hypokinesia. Thus, the time required for normalization of metabolism is not always by far proportionate to the duration of prior hypokinesia. These facts must be taken into consideration when developing rehabilitation measures and determining optimum time of return to ordinary living conditions following hypokinesia.

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HUMAN CENTRAL HEMODYNAMICS DURING LOWER LIMB DECOMPRESSION

[Article by V. V. Rumyantsev and V. Ye. Katkov]

[English abstract from source] Experiments were performed to
study the effect of leg decompression in the head-down posi-
tion at -15°. The method of chronic catheterization was used,
pressure was measured in different areas of the cardiovascular
system, blood was withdrawn for biochemical analysis. The ef-
fect of leg decompression was compared with that of lower body
negative pressure. Decompression produced changes in PAP and
CVP that were similar in sign but different in magnitude. The
decompression-induced changes in PAP and CVP were primarily
determined by the area of exposure. Using previous data, a
nomograph was constructed to evaluate PAP and CVP variations
as a function of the decompression mode and site.

[Text] Increasing significance is being attributed in recent times to in-
vestigation of the effect of local negative pressure (LNP) on human
hemodynamics [1, 5]. This is related to the extensive use of LNP in space,
sports and clinical medicine [1, 4]. Previously, the effect of this fac-
tor on various parts of the human body, with the exception of the legs,
was investigated [2, 3]. Our objective here was to test the effect of
decompression of the lower extremities on central circulation in healthy man.

Methods

These studies were conducted with the participation of healthy male subjects
(average age 34 years) who had undergone a thorough physical examination. To
perform the task set forth, we used the method of long-term implantation of
catheters in the pulmonary (Swan-Ganz) and brachial (teflon) arteries. We
used electromanometers (Siemens-746) to record central venous pressure (CVP),
pressure in pulmonary (PAP) and brachial arteries. Data were recorded on
a Mingograph-82 (Siemens-Elema). Minute volume was measured by the thermo-
dilution method; parameters of acid-base status and blood oxygenation were
determined using an AVL-940 automatic gas analyzer. The methods of investiga-
tion and equipment used were discussed in greater detail in previously pub-
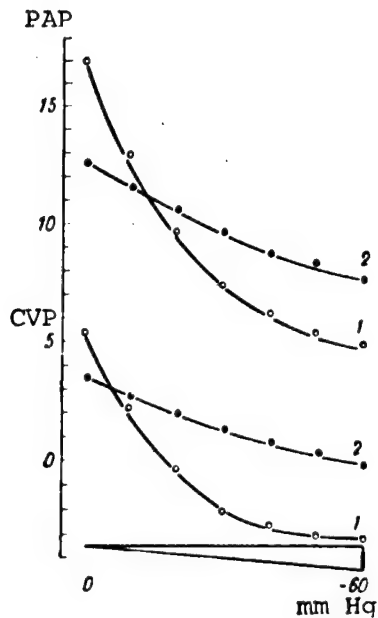lished works [1-5]. A bladder was applied to the upper third of the thigh.

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Figure 1.
Changes in PAP and CVP as related
to different modes of decompression;
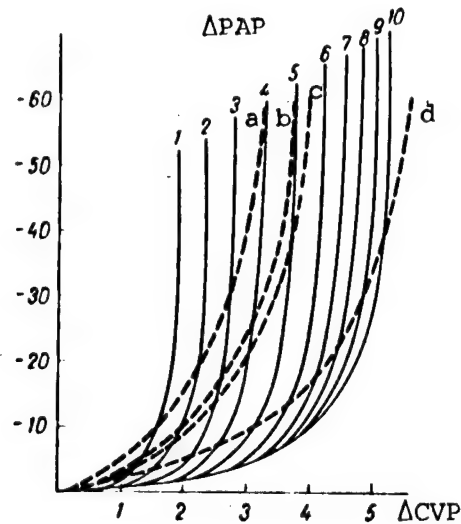x-axis, decompression (mm Hg)
1) LBNP
2) LNP

Figure 2.
Nomogram for determination of changes
in PAP and CVP with different variants
of decompression; y-axis, decompression
(mm Hg)
a,b,c) LNP applied to both legs,
        lower extremities and
        abdominal region, respectively
d) LBNP

The results were processed on a computer, and Student's   criterion was
used for statistical analysis.

The results obtained in the first series (lower body negative pressure--
LBNP) and in the second series (LNP) were compared to the baseline with
the body in antiorthostatic position (AOP) at a -15° tilt angle.

Results and Discussion

Figure 1 illustrates PAP and CVP as a function of decompression in the
transitory period (mode smoothly changed from 0 to -60 mm Hg in 3 min).
The pressure curves were obtained from the results of a test using a
previously described method [2, 5]. The obtained data revealed that the
function is described by exponent $P = P_0 + (P_b - P_0)e^{Kp}$, where P is CVP
or PAP level; P_b is baseline pressure with $P = 0$; P_0 is end (maximum)
pressure; p is decompression level; K is a coefficient with the dimen-
sionality of specific elasticity (in mm Hg^{-1}) (Footnote 1) ($K' = 100 K$).

Deviations of test data from the theoretical curve were assessed by the
relative difference between our results and theoretical values. With LBNP,
this difference constituted a mean of 17% for PAP and 14% for CVP. With
LNP, average deviation was 11% for PAP and 6% for CVP.

P_0 is attributable to maximum deposition of blood in the region submitted to
decompression. For this reason, we took for analysis results obtained on
the condition that P_0 (LBNP) < P_0 (LNP). The mean group values of P_0 and K'
in the first series are 2.61±0.89 mm Hg and 4.08±0.64 mm Hg^{-1}, respectively,

for PAP, 3.05±0.88 mm Hg and 4.07±0.22 mm Hg^{-1} for CVP; in the second series: 6.27±1.0 mm Hg and 4.65±0.9 mm Hg^{-1} for PAP, 1.11±0.75 mm Hg and 2.12±0.43 mm Hg^{-1} for CVP, respectively.

We demonstrated a correlation between P_0 with use of LNP and LBNP (K_{cor} = 0.9). No correlation was found for coefficient K. On this basis, it can be assumed that P_0 is determined mainly by the area of exposure.

Change in main parameters of circulation with use of different factors

Parameter	Factor		
	AOP	LNP	LBNP
CVP, mm Hg	3,0±1,2	0,17±0,85	−1,0±1,12
PAP_s, mm Hg	18,7±1,6	14,2±1,3	12,75±1,17
PAP_d, mm Hg	6,25±1,02	4,92±0,81	2,5±1,18
PAP_m, mm Hg	11,75±0,96	8,75±0,77	7,5±1,06
BP_s, mm Hg	112,0±4,2	110,7±4,85	115,83±4,55
BP_d, mm Hg	66,67±4,09	66,83±4,11	71,67±3,8
BP_m, mm Hg	83,17±4,21	84,33±3,87	87,17±4,25
CI, ℓ/min/m^2	3,61±0,31	3,14±0,26	2,87±0,08
SI, mℓ/m2	52,3±3,65	43,23±3,83	41,65±2,63
RVF, kg-m/min	0,97±0,18	0,81±0,11	0,86±0,14
HR/min	68,7±1,76	69,7±2,32	70,0±3,42
HbO2, %	76,93±0,85	75,47±1,12	72,0±2,1
AVDO2, vol.%	4,12±0,21	4,45±0,25	5,18±0,36

Note: Subscripts "s", "d" and "m" refer to systolic, diastolic and mean, respectively. HbO2--oxygenation of hemoglobin; AVDO2--arteriovenous difference for oxygen

After the transitional period, decompression of −30 mm Hg was maintained for 10 min. The group means recorded at the end of this period are listed in the Table. As we see, both LBNP and LNP change CVP and PAP to a greater extent than cardiac (CI) and stroke (SI) indexes; right ventricular function (RVF), heart rate (HR) and arterial pressure (BP) do not change. PAP reaches the level of the orthostatic test (8.0±1.0 mm Hg) with lower modes of decompression than CVP (−2.0±1.0 mm Hg).

A comparison to the results of the preceding studies indicates that the hemodynamic effect of P_0 with LBNP and LNP to the lower limbs and LNP to both legs is determined primarily by the area of exposure. On the basis of the obtained results (means for groups of subjects), we can plot a nomogram that would indicate the changes in PAP and CVP as a function of decompression. Figure 2 illustrates plots of decompression values (mm Hg; x-axis) and changes in CVP (y-axis). An oblique coordinate grid was plotted to find the PAP changes. The data are the means for the group of subjects and reflect well the dynamics of changes in PAP and CVP with decompression of different parts of the human body.

Thus, use of negative pressure on the lower extremities occupies an intermediate position between LBNP and decompression of both legs with regard to efficacy. The shift of parameters of central circulation with decompression of different parts of the lower half of the body is determined primarily by the area of exposure in the range of tested decompression modes.

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PHASIC PROCESSES IN KINETICS OF FORMED BLOOD ELEMENTS

[Article by V. V. Verigo and F. Gauser (USSR, CSSR)]

[English abstract from source] When quantitating blood shifts
in response to environmental effects, it is important to take
into account the phasic pattern of certain processes. Theo-
retical considerations and experimental data on the fluctua-
tions of the counts of formed elements have been published.
Since the fluctuations cannot be easily detected by experi-
mental methods, they can be investigated using mathematical
modeling. A model describing the counts of red blood cells
and their precursors in relation to the age structure of the
population has been developed. Depending on the oxygen re-
quirements and physiological parameters, humoral regulation
controls cell proliferation and release into the functioning
pool. The model allows for incidental hemolysis as well as
for life-time of red blood cells. Simulation of various pro-
cesses in the blood system when exposed to unusual environ-
mental effects has shown that some of the processes can be
phasic in character.

[Text] Functional changes in the erythron system constitute one of the reac-
tions of the human body to factors involved in long-term spaceflights. As
it has been indicated before [1], the following are observed: decrease in
red cell count, concentration of hemoglobin, prolonged reticulocyte reac-
tion, change in energy metabolism in red blood cells. Hence, it can be
concluded that spaceflights are associated with some change in hematological
status.

At the present time, the views are optimistic concerning the possibility of
adaptation of the blood system to spaceflight conditions (including long-
term ones) and complete recovery after flights. Nevertheless, it is still
a pressing task to perform a quantitative evaluation of the effects of
spaceflight factors on hematological parameters, particularly with considera-
tion of individual reactions and numerous missions by the same individual.
In order to make an adequate quantitative assessment, one must take into
consideration the possibility of occurrence of processes in the hematological
system that are phasic in response to homogeneous or continuous factors.

Unlike a number of other functional systems of the body, the condition of which can be evaluated by means of repeated and relatively frequent measurements, hematological tests are made on the basis of a considerably smaller volume of data. For this reason, it is deemed expedient to make estimates, in a number of instances, by means of mathematical models based on existing theoretical and experimental conceptions.

Mathematical models of the red blood system began to be developed about 20 years ago [10, 11, 20]. Quantitative evaluation of the process of postradiation recovery of erythron was a practical application of such models. Development of the blood system model then proceeded in the direction of both expansion of the range of material studied [4] and increase in range of investigated phenomena [2, 3, 5, 7]. The cited sources are an illustration, but are far from exhausting all of the existing literature on this subject.

The possibility of fluctuation of parameters of a number of functional systems of the body, including cellular systems, such as the hemopoietic system and functional pool of formed elements of blood, has been demonstrated both theoretically and practically, with use of a large amount of experimental data [9, 13, 14]. The fluctuating nature of hemopoiesis has been validated [17]. Examples of fluctuations in the blood system have been demonstrated in some articles [15, 16, 21, 23]. Various factors can serve as the cause of fluctuating processes. It could be interaction between processes of deposition and migration of formed elements [22], nonlinear functional connections in the system [12, 18], delay effects [8]. Some authors have discussed autofluctuation phenomena [6, 7]. The theoretically demonstrated modes were similar to those observed in reality in the presence of some types of functional hemopoietic system disorders.

Work on use of mathematical models of erythropoiesis for evaluation of effects of spaceflights on man is being done in the USSR and United States. U. S. specialists have conducted an investigation to assess the so-called anemia effect of spaceflights [9], and they used simulation models to assess the effect of hypothetical drawing of blood samples on Skylab crew members during their mission [19].

One of these authors proposed an erythropoietic model to assess the effects of spaceflight factors [2], and its distinction was that it took into consideration the age structure of red cell precursors and rate of "aging" of erythrocytes circulating in blood as a function of intensity of metabolism. We used the condition that red cells were destroyed when they reached the maximum age. As shown by the results of more recent studies [8], expressly consideration of this really occurring phenomenon makes it possible to detect fluctuations in number of formed elements over a long period. The proposed model simulated rather well the changes in erythrocyte mass in the course of a spaceflight and in the period of postflight recovery from a number of missions that had been completed by that time by Soviet and American cosmonauts. However, analysis of only the number of cells in the functional pool (erythropoietin controlled only the rate of release of reticulocytes) and several simplifications that were used diminished the adequacy of the model and its applicability to analysis of real processes.

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We have generalized this model to take into consideration processes occurring in dividing-maturing and maturing populations of red cell precursors. Here, we are not considering the pool of stem cells, since several authors have found that humoral relations had little effect on the stem cell population.

We assume that there is a two-component mixture in the functional pool of mature erythrocytes A and reticulocytes B_1, released into the blood stream due to inefficient hemopoiesis. The change in age densities of these particles can be described in partial derivatives by the following equations:

$$\frac{\partial A}{\partial t} + M \frac{\partial A}{\partial \tau} = - f_A(t, \tau) A(t, \tau), \tag{1}$$

$$\frac{\partial B_1}{\partial t} + M \frac{\partial B_1}{\partial \tau} = - f_B(t, \tau) B_1(t, \tau) +$$
$$+ \beta(t, \tau E) B(t, \tau), \tag{2}$$

where t is ordinary physical time and τ is "biological" time characterizing cell maturation; function β shows that the intensity of reticulocyte discharge depends on the concrete point in time, extent of maturity of reticulocytes and hormonal stimulation of this process; $M = \partial\tau/\partial t$ is related to intensity of metabolism--"living pace" of the cell. The quantity of dividing-maturing and maturing populations of precursor red cells B that can be identified with morphological forms from proerythroblast to polychromatophil erythrocyte is described by the equation:

$$\frac{\partial B}{\partial t} + M \frac{\partial B}{\partial \tau} = \alpha(t, \tau, K, E) B(t, \tau) -$$
$$- \beta(t, \tau, E) B(t, \tau) \tag{3}$$

The following serve as boundary conditions for equations (1)-(3):

$$A(t, 0) = B(t, 0) + B_1(t, \theta), \tag{4}$$
$$B(t, 0) = \gamma(t) c(t), \tag{5}$$
$$B_1(t, \varphi) = \beta(t, \varphi, E) B(t, \varphi), \tag{6}$$

where C is number of cells in the stem pool, $\gamma(t)$ determines the specific rate of their commitment in the direction of erythrocyte precursors.

At this stage, the mechanism of control of the commitment process is not considered, γ and C are assumed to be constant or to change according to a specified law. Boundary conditions (4)-(6) define the conditions for migration of cells between populations. Parameters φ, Θ and ψ determine the time of cessation of cell division at the stage of polychromatophil normocyte, cell maturation and its biologically maximum age, respectively. Functions $f_A(t, \tau)$ and $f_B(t, \tau)$, which describe the specific rate of death of cells in the functional pool, are considered to equal:

$$f_A = f_{A0}(1 - \tau/\psi)^p \cdot e^{-p\tau/\psi},$$
$$f_B = f_{B0} = \text{const.} \tag{7}$$

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Function $\alpha(t, \tau)$, which determines the specific rate of proliferation of "early" cells in population B, takes into consideration humoral factors K and E (chalonic and erythropoietic).

In accordance with 5, we assume that α has the following appearance:

$$\alpha = \alpha_0(t, \tau)\ \frac{eE(t - t_e)}{1 + K},\tag{8}$$

$$\text{where} \qquad K = b \int_0^\theta B(t, \tau)\, d\tau\tag{9}$$

(ϵ is the coefficient of influence of erythropoietic).

Parameter t_e is indicative of a lag in the chain of erythropoietin action.

The intensity of production of erythropoietic E, by analogy with [2], can be conceived of as a function of relation of current hematocrit Ht to its nominal value and difference between oxygen uptake, proportionate to level of metabolism M, and its transport by functional pool cells:

$$E = e_0 - e_1 \frac{Ht}{Ht_0} + e_2(\mu M - UHB).\tag{10}$$

$$UHB = \frac{0.0139}{VP}\ \left| \int_q^\theta B(t, \tau) g_B(t, \tau)\, d\tau + \right.$$
$$\left. + \int_\theta^\Psi A(t, \tau) g_A(t, \tau)\, d\tau \right|\tag{11}$$

In the above equations, e_0 is a certain "stationary" value for erythropoietin production, e_1, e_2 and e are coefficients of proportionality, μB is oxygen taken up, UHB is transported amount of oxygen.

UHB as a function of total concentration of hemoglobin is approximate. A more precise analysis requires consideration of concentrations of bicarbonates in extracellular fluid, pH of arterial blood and certain other parameters of the system of acid-base equilibrium.

Functions g_A and g_B describe the cell's capacity to transport oxygen, aside from its use to maintain its own vital functions. The difference between these functions takes into consideration the greater energy expended by reticulocytes, as compared to erythrocytes. In addition to control of size of population B, erythropoietin also controls migration into the functional pool of B cells that have not reached maturation time Θ:

$$\beta = \beta_0(t, \tau) \cdot \beta_1 [E(t - t_e) - E_0]\tag{12}$$

Having specified the values for structural parameters of functions t, g, K, α, β and other controlling factors, we can simulate a broad spectrum of situations in the erythron system and provide greater universality to the

submitted version of the mathematical model, as compared to previously used versions. The distinctive feature of the modes we found is the phasic change in number of formed elements of blood. The presence of regression in the system is closely related to the type of function $t_A(t\tau)$, which was chosen here in accordance to results of experiments in the form of γ-distribution or a type III Pearson curve.

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MORPHOLOGICAL AND BIOCHEMICAL INVESTIGATION OF RAT ADRENOCORTICAL FUNCTION DURING LONG-TERM HYPOKINESIA

[Article by Ye. V. Vorotnikova and Ye. A. Zagorskaya]

[English abstract from source] Female rats exposed to 3-month hypokinesia were used to study adrenal morphology and plasma corticosterone. Prolonged hypokinesia (60-90 days) led to a dissociation between adrenal hypertrophy and lower corticosterone content in plasma. During hypokinesia rats were also exposed to an additional stress-effect, i.e., 5-hour immobilization. This approach showed that in the course of 90-day hypokinesia the adrenal cortex retained its ability to react to an acute stress by an enhanced corticosteroid secretion. Moreover, in response to stress-effects of identical strength and duration the experimental adrenals produced more corticosterone than the controls with no structural rearrangement or delipoidization.

[Text] The results investigations pursued in recent years indicate that long-term hypokinesia elicits chronic stress in man and animals [3], the process of adaptation to which is associated with appreciable changes in the hypothalamo-hypophyseo-adrenal system [9, 13, 19, 22].

Our objective here was to conduct a combined morphobiochemical study of structure and function of the adrenal cortex of rats submitted to long-term hypokinesia, as well as to determine the reserve capacities of the adrenal cortex by using an additional stressor during hypokinesia.

Methods

This study was conducted on 250 mongrel female rats initially weighing about 170 g. Hypokinesia was produced by placing the rats in individual box-cages. Acute stress was produced by 5-h immobilization of rats in extended prone position on special tables [18]. The animals were divided into 6 groups: the 1st consisted of the vivarium control (70 rats), the 2d--control animals submitted to acute stress (60 rats), the 3d--rats submitted to hypokinesia (50 rats), the 4th--animals submitted to acute stress during hypokinesia (50 rats), the 5th--rats during a 1-month recovery period after hypokinesia

(10 animals) and the 6th--rats submitted to acute stress in the recovery period (10 animals).

We examined the adrenals and blood plasma. The animals were decapitated at the start of the experiment (baseline control),after 1 and 2 weeks, 1, 2 and 3 months of hypokinesia, as well as 1 month after it (recovery period). The rats (8-10 from each group) were decapitated at the same time of day (1400-1500 h). We weighed the animals and, during necropsy, the adrenals. One adrenal was fixed in 10% neutral formalin and imbedded in histoplast. Adrenal sections 4-5 μm thick were stained with hematoxylin and eosin, and astrin which enabled us to demonstrate differentially functionally active and inactive cells on the basis of differences in staining of their nuclei (the nuclei of functionally active cells are stained blue with this dye and those of functionally inactive cells, red) [10, 16]. The other adrenal was frozen in dry ice. Adrenal sections 10 μm in thickness were prepared in a cryostat and used for demonstration of lipids, staining them with Sudan black B and oil red 0.

For quantitative estimation of changes in adrenocortical cell activity, we counted 500 nuclei at a time in astrin-stained sections, in the top layer of the fascicular zone and determined the ratio between active and inactive cells.

We assayed plasma concentration of corticosterone by the radioimmune method developed by P. F. Brenner [11] and modified by N. P. Goncharov et al. [1]. The standard solution of tritium-labeled corticosterone, lyophilized antiserum to corticosterone and nonradioactive corticosterone standard were obtained from the Institute of Experimental Pathology and Therapy, USSR Academy of Medical Sciences. Radioactivity was counted using the Delta-300 liquid scintillation counter of the Tracor Europa Firm with efficacy of tritium count of about 57%. The digital data were submitted to statistical processing according to Student.

Results and Discussion

The weight of rats submitted to hypokinesia was considerably lower than that of control animals (Figure 1a). After hypokinesia, this parameter grew rapidly, coming close to the level in control animals after 1 month of recovery without, however, reaching the latter.

Starting on the 7th day of hypokinesia, the absolute weight of the adrenals did not differ from control animals, with exception of the 30th day. This is indicative of relative adrenal hypertrophy in experimental rats, since they weighed considerably less than controls. For this reason, the relative weight of the adrenals was 20-40% more than in the control at all stages of hypokinesia (with the exception of the 7th day (Figure 1b and c). After 5-h exposure to the additional stressor, no increase in adrenal weight was demonstrable in either experimental or control rats.

Histological examination of the adrenals revealed that already 7-day restriction of motor activity leads to hypertrophy of the fascicular zone and increase in active cells in it. The increase in number of functionally active cells and dilatation of the fascicular zone of the adrenal cortex persisted
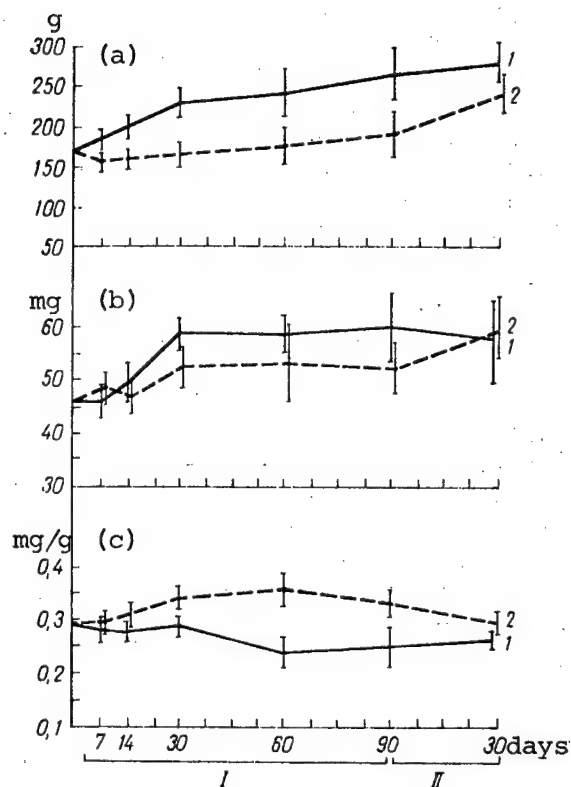
Figure 1.
Changes in body weight (a), absolute (b) and relative (c) weight of rat adrenals during and after long-term hypokinesia
Here and in Figure 3, x-axis:
I) days of hypokinesia
II) days of recovery period
1) control
2) hypokinesia

Vertical segments--95% confidence intervals

throughout the hypokinetic period. After 7 days of hypokinesia, the entire reticular zone and lower third of the fascicular zone were wanting in lipids, whereas droplets of fat appeared in the subglomerular layer (Figure 2б). After 14 days, delipoidization of the cortex diminished, and on the 30th day we observed accumulation of lipids in all cortical zones (Figure 2в). There was normalization of lipid content in the adrenal cortex after 60 and 90 days of hypokinesia (Figure 2г).

Acute stress did not elicit structural changes in the adrenal cortex of rats submitted to hypokinesia. On the 7th, 14th and 30th days of hypokinesia, the additional stressor elicited delipoidization of the cortex, but to a much lesser extent than in control animals. With increase in duration of hypokinesia to 60 and 90 days, the acute stressor ceased to elicit a change in lipid content of the adrenal cortex, suggesting that the adrenals of experimental rats did not react to the additional stressor. One month after hypokinesia, there was the same degree of delipoidization of adrenals of experimental and control animals in response to 5-h immobilization stress, and it invoved the reticular and lower half of the fascicular zone.

Plasma corticosterone concentration was in the range of 35-40 μg% in control rats (Figure 3), which is consistent with the data of a number of authors who demonstrated that female rat blood corticosterone level is 2.5-3 times higher than in males [7, 9, 17, 24], ranging from 10 to 60 μg% in the course of a 24-h period, reaching maximum values at 1500-1600 h [4, 12, 14, 15, 25, 26]. On the 7th day of hypokinesia, corticosterone level was 47% higher than in the control. Thereafter, the concentration diminished. On the 14th day of hypokinesia, the level of this hormone in blood reached the control value, whereas on the 60th and 90th days it decreased by 31 and 39%, respectively (see Figure 3). One month after hypokinesia, plasma corticosterone content reverted to the control level.

The increase in blood corticosterone content in response to the acute stressor was the same in animals submitted to hypokinesia and control rats. It is only after 3-month restriction of motor activity that the plasma hormone level was 42% higher after additional stress than in stressed control animals.

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This distinction of adrenocortical reaction persisted in the recovery period, although the differences were less marked (see Figure 3).
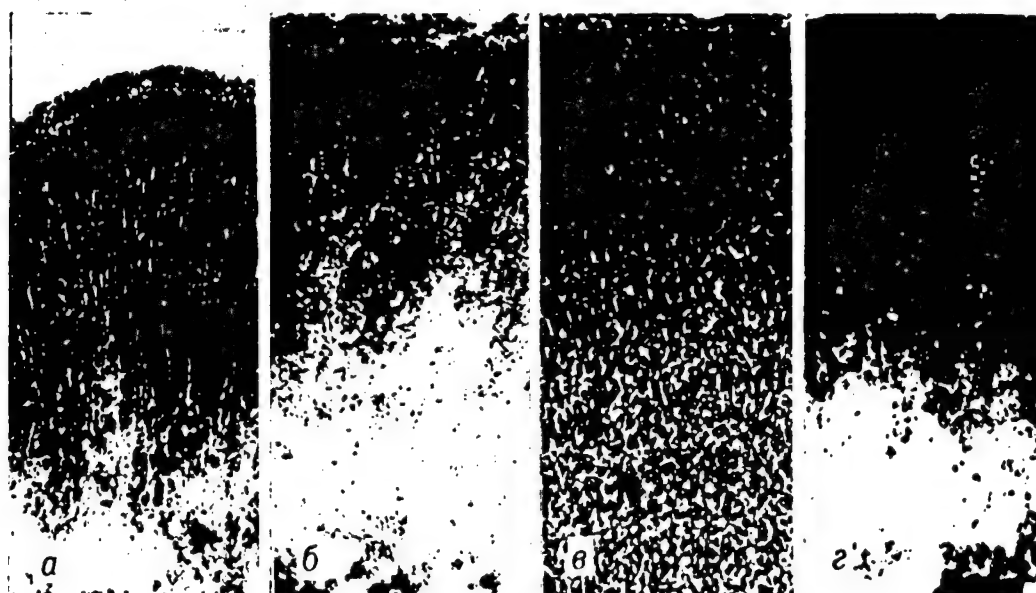

Figure 2. Lipids in rat adrenal cortex at different stages of adaptation to hypokinesia. Sudan black B, lens 3.5×, eyepiece 7× magnification
а) control
б) delipoidization of adrenal fascicular cells on 7th day of hypokinesia
в) accumulation of lipids in adrenal cortex after 1 month of hypokinesia
г) normalization of lipid content in adrenal cortex after 2 months of hypokinesia
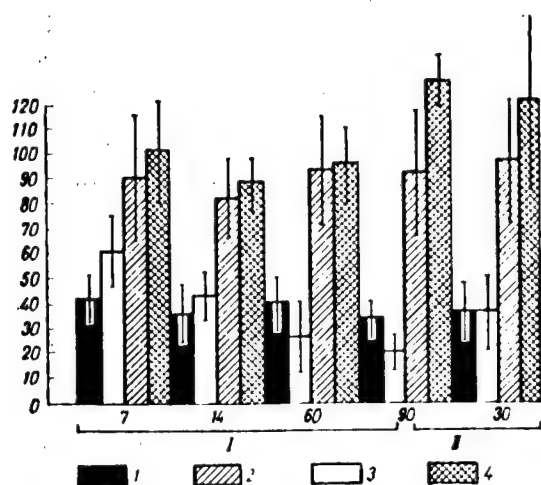
Figure 3.
Corticosterone content (μg%) in rat blood plasma
1-4) 1st-4th groups of animals, respectively

The results of this study confirmed the numerous reports to the effect that animal exposure to strict hypokinesia elicits phasic changes in the adrenals inherent in chronic stress [3, 8]. The first month of hypokinesia, when an increase in blood corticosteroid content and hypertrophy of the adrenal cortex were observed, corresponds to the anxiety stage of the general adaptation syndrome (GAS) [23]. As the duration of hypokinesia increased, the anxiety stage of GAS was replaced by the resistance stage. It was characterized by dissociation between hypertrophy of the adrenal cortex and decrease in plasma corticosterone content. Other authors [22] have also observed a decline of blood corticosterone level in rats submitted to

chronic stress. The decrease in concentration of this hormone during long-term hypokinesia could be related to inhibition of ACTH secretion [20] or increase in corticosterone catabolism. The decline of blood corticosterone level in rats under chronic stress is instrumental in intensifying ACTH production on the feedback principle [5, 22], and it is one of the causes of hypertrophy of the adrenal cortex. The latter, in turn, could be associated with diminished sensitivity of steroidogenic cells to ACTH and, consequently, decrease in corticosteroid secretion [5, 6].

In spite of the prolonged hypokinesia, we failed to demonstrate morphological or functional signs of the depletion stage in our experiment.

Investigation of reserve capacities of the adrenals of rats submitted to hypokinesia revealed that the additional stressor led to the same or even greater (90th day) increase in plasma corticosterone content, as compared to the control. Considering that the base level of this hormone in blood of rats submitted to hypokinesia for 60 and 90 days was lower (see Figure 3) than in control animals, it can be concluded that the adrenals of rats adapted to hypokinesia produce more corticosterone in response to a stressor of identical strength and duration than the adrenals of control animals. Analogous changes under chronic stress were demonstrated by other authors [2, 22]. The stronger reaction to additional stress of experimental animals, as compared to the control, is apparently indicative of occurrence of some changes in regulatory mechanisms of the hypothalamo-hypophyseo-adrenal system.

We have already mentioned that the increase in corticosterone production by adrenals of rats submitted to hypokinesia in response to an acute stressor was not associated with marked structural change and depolarization of their cortex. This fact is indicative of an increase in reserve capacities of adrenocortical steroidogenic tissue that had been hypertrophied during hypokinetic stress. The possibility of secretion of high amounts of corticosteroids by adrenals of rats submitted to chronic stress combined with additional burdens, without appreciable morphological changes, is confirmed to some extent by the studies of G. G. Nussdorfer [21]. He demonstrated that, in the course of adaptation to chronic stress, there is not only an increase in number of fascicular cells in the adrenal cortex, but activation of the process of steroidogenesis in each of these cells. As a result, corticosterone production may increase dramatically in response to an additional stimulus.

Investigation of the functional state and reserve capacities of adrenals of rats adapted to prolonged hypokinesia enabled us to establish the following: long-term (60-90 days) hypokinesia is characterized by dissociation between adrenal hypertrophy and decrease in plasma corticosterone content; in the course of 90-day hypokinesia, the adrenal cortex retains the capacity to respond to acute stress by increasing corticosteroid secretion and, consequently, no depletion of adrenal function is observed; the reserve capacities of steroidogenic tissue of the adrenal cortex increase with 90-day hypokinesia: the cells of the fascicular zone acquire the capacity to produce higher amounts of corticosterone without structural change and delipoidization of the cortex; the increase in sensitivity of steroidogenic adrenocortical tissue of rats submitted to long-term hypokinesia is indicative of changes in mechanisms of its regulation.

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EFFECT OF DIPHOSPHONATES ON BONES OF HYPOKINETIC RATS

[Article by V. N. Shvets, A. S. Pankova, O. Ye. Kabitskaya, Z. Ye. Vnukova
and B. V. Morukov]

[English abstract from source] The diphosphonate effect on
bones was studied in Wistar male rats weighing about 200 g.
The rats were kept for 60 days in small-size cages where their
motor activity was diminished. Every day the rats were given
per os 0.3% solution of 1-hydroxy-ethylene-1,1-diphosphonate
(HEDP) containing 9 mg/kg phosphorus. In the course of hypo-
kinetic exposure the rats developed generalized osteoporosis.
Histomorphometric measurements demonstrated that the drug did
not prevent mineral losses from the tubular bones (humerus,
femur). However, the drug led to a complete bone mass recovery
in the pelvix and a partial recovery in the sternum. The drug
also produced a preventive effect on the population of cells-
precursors of osteogenesis the number of which decreases sig-
nificantly during hypokinesia.

[Text] At the present time, researchers are devoting increasing attention
to diphosphonates (synthetic analogues of pyrophosphates) as effective means
of treating and preventing osteopathies and disturbances referable to mineral
metabolism (osteoporosis of diverse etiology, Paget's disease, myositis ossi-
ficans, nephrolithiasis and others). Unlike pyrophosphates found in biological
fluids and bones, diphosphonates are resistant to enzymes (pyrophosphatase
and polyphosphatase), which makes it possible to take them by mouth [5-7, 17].
It has been established that the nature of diphosphonate effects on bone is
largely determined by their chemical structure [17]. For example, mono-
potassium salt of 1-hydroxyethylene-1, 1-diphsophonate (HEDP) or, as it is
also called abroad, disodium salt of ethane-1-hydroxy-1,1-diphosphonate, has
a selective effect on mineralization, causing its inhibition, while dichloro-
methane diphosphonate and 3-amino-1-hydroxypropane-1,1-diphosphonate reduce
bone resorption. All three diphosphonates are used in clinical practice for
various disturbances of mineral metabolism [5-7, 17].

We still do not know whether HEDP can prevent development of osteoporosis
arising when motor activity is restricted (hypokinesia). Our objective
here was to investigate this matter.

Methods

We used 39 male Wistar rats with baseline weight of about 200 g in the experi-
ments. One group of animals was kept in box-cages (hypokinesia) for 60 days
and the other, under the usual vivarium conditions (control). Throughout the
experiment, both groups of animals were given a neutral agent (placebo)
administered through a probe into the esophagus. In addition, some rats
in both groups were given 0.3% HEDP solution daily (9 mg/kg phosphorus). At
the end of the experiment, the rats were decapitated and their sternum, innomin-
ate bones, humerus and femur were excised. In addition, we extracted marrow
from the iliac bone and different doses of the marrow (from 0.6 to $2 \cdot 10^6$ cells)
were subsequently cultured in vitro on medium 199 with 20% embryonic calf serum
[3]. We measured the length of the long bones with calipers. The bones were
fixed in a mixture of 5% formalin and Muller's fluid. They were then decalci-
fied in 5% nitric acid and imbedded in paraffin. Frontal histological bone
sections 5-7 μm thick were prepared and stained with hematoxylin and eosin
or toluidine blue. We evaluated the condition of spongy bone using an
ocular micrometer (linear parameters) or a 0.5 mm mesh test grid (volumetric
parameters). Polynuclear osteoclasts were counted in the entire area occupied
by primary spongiosa at a magnification of 400×. To assess long bone growth
in width, we prepared transverse sections 20 μm thick in a very specific
part of the diaphysis using a freezing microtome. We outlined the projection
of each section (cross section and medullary canal) three times using a
photo enlarger, with subsequent planimetry.

All digital data were submitted to variational statistical processing using
Student's t criterion.

Results and Discussion

The lengthwise growth rate of bones decreased by about 5-6% during hypokinesia,
as compared to the norm. Under the same conditions, we observed thinning of
the diaphyseal cortical plate with retention of area of the medullary canal
at the control level. These findings indicate that inhibition of widthwise
bone growth is due more to depression of periosteal osteogenesis than to
increased bone resorption by the endosteum. HEDP had no positive effect on
either parameter.

Table 1 shows that there is statistically reliable decrease in volume and
extensiveness of spongiosa in the humeral metaphysis during hypokinesia. In
addition to bone, cartilage also underwent substantial changes: decrease in
epiphyseal growth plate (EGP), amount of cartilage in primar- and secondary
spongiosa and in degree of its spread in the diaphyseal cavity. Concurrently
with the reduction in volume of the spongiosa there was proportionate decrease
in number of osteoclasts. As a result, the number of these cells per 1% bone
mass was the same as in the control. HEDP, which did not affect the para-
meters of the humerus in experimental rats, had an unexpected effect on the
spongiosa of control animals. Thus, under the influence of HEDP, we observed
a tendency toward increase in mass of spongiosa and statistically reliable
increase in number of osteoclasts, which could be indicative of activation
of the process of bone resorption. However, it is known that, with use of
HEDP and other diphosphonates, increase in the osteoclast population of
the metaphysis of normal rats is not necessarily related to increase in their

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functional activity and, consequently, intensification of resorption [10, 11].
In our case too, osteoclasts presented low activity: they often lost a connec-
tion with the surface of osseous trabeculae   and their cytoplasm was less
oxyphilic.

Table 1.   Parameters of spongiosa in proximal end of humeral diaphysis (M±m)

Parameter	Vivarium control (10)	Hypokinesia (9)	Vivarium control + HEDP (5)	Hypokinesia + HEDP (5)
Volume of entire spongiosa, %	30,72±1,57	12,87±1,2	38,84±2,63	17,54±1,7
Volume of primary spongiosa, %	48,0±5,4	32,0±5,2	56,4±2,08	26,9±2,7
Depth to which spongiosa pene- trates into medullary canal,mm	3,6±0,23	2,67±0,2	4,32±0,42	2,74±0,28
Volume of cartilage in entire spongiosa, %	14,88±1,0	3,72±0,42	17,1±1,35	3,2±0,54
Volume of cartilage in primary spongiosa, %	24,6±2,0	18,5±1,8	28,5±2,4	18,0±1,5
Width of EGP, μm	187,0±2,3	144,0±5,8	179,0±3,7	140,0±4,4
Number of osteoclasts in primary spongiosa	75,0±6,6	52,0±6,3	141,0±5,2	42,0±5,6

Note: Here and in Table 2, differences between experiment and control in
        Tables 2-4 in parentheses are statistically reliable for all para-
        meters[sic].   Number of animals is also given there.

Table 2.   Parameters of spongiosa of distal end of femoral diaphysis (M±m)

Parameter	Vivarium control. (12)	Hypo- kinesia (16)	Vivarium control + HEDP (6)	Hypokines. + HEDP (5)
Volume of entire spongiosa, %	27,13±0,7	9,4±0,35	26,6±1,46	11,22±1,04
Volume of primary spongiosa, %	48,3±1,3	17,6±1,2	56,0±1,45	17,0±1,8
Depth to which spongiosa pene- trates into medullary canal, mm	5,73±0,36	2,95±0,12	5,9±0,53	3,75±0,2
Volume of cartilage in entire spongiosa, %	14,94±0,34	2,43±0,11	22,6±1,0	2,62±0,36
Volume of cartilage in primary spongiosa, %	24,7±1,7	14,8±1,45	27,0±2,2	16,0±1,6
Width of EGP, μm	190,0±2,0	131,0±8,3	200,0±2,8	154,0±4,8
Number of osteoclasts in primary spongiosa	120,0±12,0	33,0±3,7	142,0±14,0	30,0±5,0

The results listed in Table 2 indicate that all parameters of the femur were
reduced under hypokinetic conditions.   Administration of HEDP did not even
have a partial protective effect on this bone.   As in the humerus, we observed
a tendency toward elevation of some bone parameters in the control group of
animals.

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In evaluating the condition of both bones, it can be concluded that osteoporosis was more marked in the femur during hypokinesia, and this direction of change also persisted with administration of HEDP. Analysis of the spongiosa is of interest. The latter usually consists of bone and cartilage. Quantitative evaluation of total trabecular weight and then separate consideration of cartilage alone (cartilagenous cores) enable us to determine the volume occupied by bone. We found that the ratio between these tissues was normally 1:1 in both bones. Under hypokinetic conditions, this ratio was dramatically impaired in favor of bone and was about 2.5:1, while administration to experimental rats of HEDP led to even more dramatic change in this parameter, which constituted 4.5:1. This imbalance between the two tissues in the presence of loss of total weight of spongiosa under hypokinetic conditions could be indicative of two factors: inhibition of "migration" of cartilage into the spongiosa due to diminished functional activity of EGP and slowing of lengthwise bone growth; intensification of ossification of remaining cartilage, which could be a compensatory reaction to widen the area of the reservoir for Ca salts. The purpose of this process is apparently to augment the Ca reserve under hypokinetic conditions when there is intensive loss of Ca in urine and feces, in order to subsequently use it in case of acute need (for example, upon termination of hypokinesia or in the presence of additional factors).

Table 3. Volume (%) of spongiosa in sternum and pelvic bones (M±m)

Type of bone	Vivarium control (12)	Hypo-kinesia (15)	Vivarium control + HEDP (6)	Hypokinesia + HEDP (6)
Sternum	18,9±0,26	14,0±0,4*	18,2±0,4	15,3±0,3*
Ilium	14,0±0,4	8,8±0,26*	15,2±0,63	14,2±0,6

Note: Here and in Table 4, the asterisk indicates statistically reliable differences between experiment and control.

Table 3 shows that the volume of spongiosa in the sternum and pelvic bones decreased in about the same proportion under hypokinetic conditions. As compared to long bones, these bones presented less marked osteoporosis. Thus, while loss of trabecular mass in long bones constituted 60-70% of the norm, in the sternum and bones of the pelvis it was only 30-40%. HEDP partially prevented loss of bone weight in the sternum and eliminated osteoporosis entirely from the ilium. Recovery of bone mass in the pelvis under the effect of HEDP is perhaps related to increase in osteogenetic function of bone marrow. Table 4 shows that HEDP increased by about 2 times the number of osteoblast precursor cells, as identified by their capacity to form phosphatase-positive colonies [3]. HEDP also restored in part the number of other stromal precursor cells localized in the ilium.

In the existing literature, the effect of HEDP was studied mainly after giving it to animals hypodermically. Since only 1-5% of the administered

dose is absorbed in blood with oral intake of this agent [1, 2], it can be assumed that 9 mg/kg HEDP taken by mouth corresponds to a dose of 0.1-0.5 mg/kg given by hypodermic injection. On this basis, we are justified in discussing our findings as related to the data in the literature obtained on animals. Several authors established that hypodermic injection of HEDP in doses of 0.001 to 1 mg/kg to normal rats did not elicit appreciable changes in bone tissue, as compared to intact animals. Merely minimal decline in rate of bone turnover, process of resorption, activity of osteoclasts (with moderate increase in their number) were observed. At the same time, there was no change in linear growth of long bones, width of EGP, volume of spongiosa, bone formation and its mineralization [8-12, 14-16].

Table 4. Number of stromal precursor cells in marrow of ilium per 10^6 explanted karyocytes (M±m)

Parameter	Vivarium control	Hypokinesia	Hypokinesia HEDP
Total number of stromal precursor cells (phosphatase-positive and phosphatase-negative cell colonies)	97,1±4,2	38,2±3,15*	58,2±6,9*
Number of osteoblast precursor cells (phosphatase-positive cell colonies)	45,8±4,0	14,0±2,7*	33,4±7,4

Conversely, large doses (5-40 mg/kg) of HEDP elicited significant changes in the animals' bone, which consist of inhibition (by about 2 times) of the process of mineralization of both spongy and compact bone, as a result of which there is an increase in volume of de novo formed osteoid. In addition, there is decrease in resorption and synthesis, depression of linear growth of bone with concurrent increase in in EGP width. Although the number of osteoclasts and nuclei in them increase, osteoclast activity diminishes appreciably (they lose their bristled fringe, the number of lysosomes decreases, there is deposition of Ca salts in the mitochondrial matrix, etc.), whereas the number of osteoblasts decreases and there is inhibition of Ca release from bone [4-8, 10, 11, 13, 15, 16, 18, 19].

If we compare our findings to data in the literature, it is easy to see that the reaction of the spongiosa of long bones of control and experimental animals is generally similar to the one observed with administration of low doses of HEDP. Our findings revealed that a low dose of HEDP has a beneficial effect on spongy bones of the pelvis under hypokinetic conditions. This local effect of HEDP is perhaps due to less marked osteoporosis and large amount of spongiosa in this bone, as compared to long bones. Bearing this in mind, as well as the fact that the spongiosa is referable to the rapidly renewed fraction of bone, it can be assumed that it is expressly in pelvic bone that there is greater accumulation of diphosphonates. As a result, HEDP can have a cumulative effect, even when used in small doses.

On the whole, the results of this investigation indicate that monopotassium salt of HEDP in a dosage of 9 mg/kg weight is not effective enough in preventing

systemic osteoporosis in hypokinetic rats. Its local preventive effect on Pelvic bones is perhaps related to the distinctions of metabolism and histogenesis of this bone.

We believe that the therapeutic effect of HEDP and other diphosphonates (of which there are presently about 30) [17] will be largely determined by the chemical structure, dosage, duration and mode of administration, on the one hand, and initial state of bone, level of mineral metabolism, as well as severity of osteoporosis and its clinical manifestations, on the other hand.

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EXPERIMENTS WITH DEVELOPING PLANTS ABOARD SALYUT-5, SALYUT-6 and SALYUT-7 ORBITAL STATIONS

[Article by L. N. Kostina, I. D. Anikeyeva and E. N. Vaulina]

[English abstract from source] The experiments with air-dry Crepis capillaris seeds flown on the spacecraft Soyuz-16 and orbital stations Salyut-5, Salyut-6 and Salyut-7 showed that the number of aberrant cells in the seedlings grown during flight (experimental) and after flight (flight control) was higher than in the ground-based control. This number was greater in the experimental seedlings than in the flight controls. The plants Arabidopsis thaliana grew from cotyledons to flowers during flight. The seeds developed postflight exhibited a lower fertility and a higher frequency of recessive mutants (Experiment Svetoblock-1). The greater number of mutants persisted in the progeny of plants that completed their developmental cycle (Experiment Phyton-3). Inhibited viability of germs manifested as a reduced germination rate of flown seeds and a premature death of seedlings. In the first postflight generation the lesions produced by large chromosome aberrations were eliminated and the lesions caused by gene mutations and microaberrations were retained.

[Text] Several previous experiments demonstrated a decline in viability and rise in incidence of mutations in plants grown on earth from seeds flown in space [9, 10]. There was a direct relationship between the observed phenomena and time that seeds were kept in space.

We report here on an investigation of the effects of spaceflight conditions on incidence of chromosome aberrations in seedlings as related to different seed-storage time in flight prior to germination, viability and mutability of plants that developed during spaceflights.

Methods

These investigations were pursued on the Soyuz-16 satellite craft and Salyut-5, Salyut-6 and Salyut-7 orbital stations (OS). Figure 1
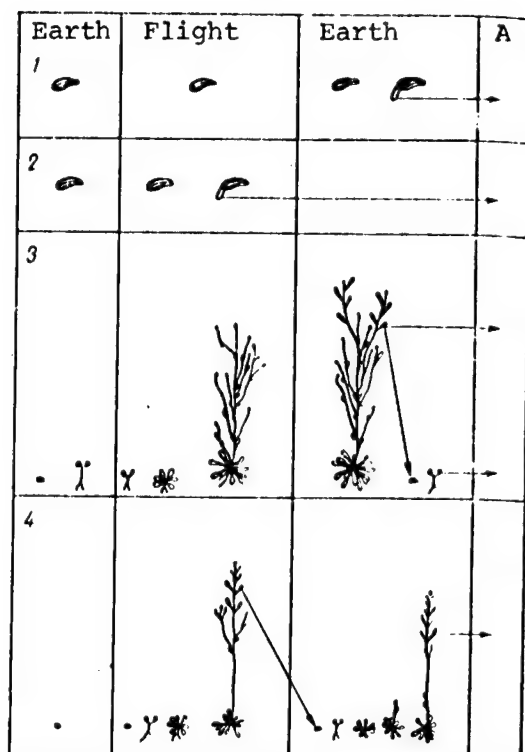
Earth	Flight	Earth	A
1			
2			
3			
4			

Figure 1.
Diagram of experimental protocol
and analysis (A) of material
  1) C. capillaris flight control
  2) C. capillaris, experiment
  3) A. thaliana, experiment in
     Svetoblok instrument
  4) A. thaliana experiment in
     Phyton instrument

illustrates the experimental set-up. We
used Crepis capillaris (L) Wallr seeds.
We placed packets of air-dried seeds in
one of the cartriges of the Biofiksator-G
instrument [1] (flight control). In the
other cartridges, after inflight storage
for 3-234 days, the seeds were soaked,
germinated in a Biotherm-4 instrument at
a temperature of $24\pm0.1°C$ and fixed (experi-
ment). Upon return to earth, the seeds of
the flight control and, concurrently, the
laboratory control were soaked, germinated,
fixed and examined similarly to the experi-
mental variant using standard methods [11].
Seeds stored for the same periods of time
on the ground served as the laboratory
control. We assessed the cytogenetic ef-
fect of flight factors on the basis of
incidence and spectrum of chromosome aber-
rations in the root meristem of seedlings.

We used Arabidopsis thaliana (L) Heynh for
experiments with vegetating plants; they
were raised in Svetoblok-1 [light-unit]
and Phyton-3 instruments [7, 8]. Both
instruments allowed the plants to grow
under sterile, airtight conditions on
agarized nutrient medium [4]. A daylight
fluorescent lamp provided plant illumina-
tion of $2-4\cdot10^3$ lux in Svetoblok-1 and
about $7\cdot10^3$ lux in Phyton-3.

Two analogous experiments lasting 65 days
were performed in Svetoblok-1. The seeds
were planted in the laboratory, they were delivered aboard Salyut-6 as seed-
lings at the stage of two cotyledonous leaves. In the first experiment, the
seeds were exposed to light for 12 h/day and in the second, 14 h/day for 16
days and then around the clock. After the flight, the plants were further
cultivated in the laboratory to the fruit-bearing stage with around the
clock illumination of about $5\cdot10^3$ lux. We examined fertility and incidence
of recessive mutants in these plants by the embryon-test method [4].

In the Phyton-3 instrument, seeds were planted on nutrient medium while in
weightlessness aboard Salyut-7. The plants were exposed to light around the
clock. The experiment lasted 69 days.

Seeds that germinated in flight were transplanted in the laboratory. In
plants that developed from them we tested fertility and incidence of recessive
mutants. Thus, plants that grew in flight were submitted to genetic analysis
and analysis for fertility in experiments conducted in Svetoblok-1, whereas
in the Phyton-3 experiment we examined offspring (first generation) of plants
grown in space. The temperature was in the range of $18-24°C$ during the

experiment and in the control. We assessed the effects of spaceflight on viability on the basis of germination of seeds gathered from plants grown in flight and according to survival of plants that developed from them. The genetic effect of flight factors was assessed on the basis of incidence of recessive lethal and pigmented mutants, as well as plant fertility.

Results and Discussion

The results of the experiments with C. capillaris seeds revealed that the level of cells with chromosome aberrations was virtually constant in all flight variants (Figure 2). In the flight variants, we observed some increase in incidence of such cells with increase in flight duration, but it was not statistically reliable. The same slope of the curves is indicative of gradual, though very slight, accumulation of potential lesions in meristem cells due to flight factors. Experiments with dry seeds have shown that this process is more intensive in the case of longer storage [9].
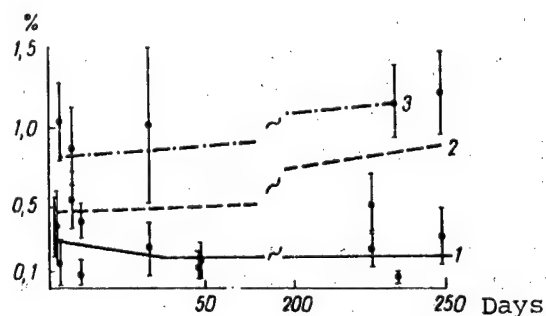
Figure 2.
Incidence of aberrant cells in root meristem of C. capillaris seedlings
  X-axis, duration of flight(days)
  1) laboratory control
  2) flight control
  3) experiment

Both flight variants exceeded the laboratory control in incidence of aberrant cells.

The higher level of aberrations in cells of seedlings that developed and were fixed in flight indicates that actively developing systems are more sensitive to flight factors. The difference in sensitivity of active and dormant systems can be attributed to two causes. On the one hand, as we know, the phases of the cell cycle differ in chromosome sensitivity to diverse factors ($G_1 < S < G_2$) [3]. In air-dried seeds, meristem cells are exposed to the factors at the G_1 phase, whereas in germinated seeds they are exposed at all subsequent phases. On the other hand, in weightlessness there is depression of repair processes, and this applies more to active systems than dormant ones [5, 6]. In all likelihood, these two mechanisms act concurrently.

On the basis of these theses, it is easy to explain the persistence of the same differences in incidence of aberrant cells between the experimental and flight control variants for the 234 days. Regardless of duration of inflight seed storage before soaking them, the duration of the more sensitive period between the time the seeds are soaked and seedlings fixed was the same in the experimental variant (46-48 h).

Analysis of the spectrum of structural mutations in the analyzed specimens from the experimental and control variants failed to demonstrate a noticeable difference in ratio of incidence of isolocus breaks and aberrations of the chromosome and chromatid types. Virtually all aberrant cells presented

a single structural chromosome aberration. It is only after storage for 234 days that we observed 3 cells with two aberrations each.

Arabidopsis plants grown in flight retained the normal phototropic reaction. The morphology of both vegetative and generative organs of experimental plants presented no appreciable deviations from the control, although their development was somewhat retarded [7, 8]. The plants placed in the Svetoblok-1 instrument did not set seeds in flight, but on earth they bloomed and bore fruit. The lack of fruit-bearing in these experiments is attributable to a shortage of light in the vegetation period, as confirmed by the results of the experiment in Phyton-3, where the plants bore fruit normally.
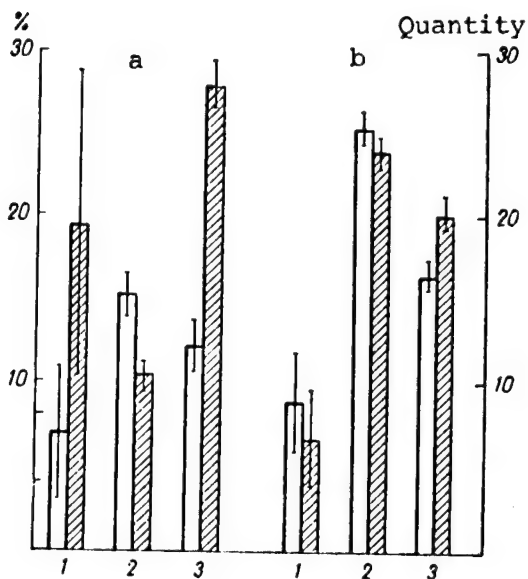
Figure 3.
Fertility and incidence of mutants in A. thaliana plants raised in flight (a) and their offspring (b)
  1) number of sterile fruit (%)
  2) number of seeds per fruit (quantity)
  3) number of mutants (%)
  White bars, control; striped, experiment

Analysis of fruit from plants raised in flight in Svetoblok-1 revealed a noticeable increase in incidence of recessive mutants and some decline of plant fertility (Figure 3). Germination of seeds taken from these plants was low (96.9% in experiment 1 and 89.3% in experiment 2), as compared to the control (99.5%).

In the Phyton-3 experiment, germination of seeds from plants raised in space and survival rate of the next generation of plants from these seeds were lower than in the laboratory control. The morphological changes were referable only to size of hypocotyls and cotyledons [8]. Fertility of these plants did not differ from the control; however, the incidence of mutants was somewhat higher in the experiment than in the control (see Figure 3).

In three experiments with plants vegetating in flight, we observed good reproducibility of results. We were impressed by the rather high incidence of mutants both in plants that developed in flight and in their offspring, as well as the corresponding controls. It should be noted that the incidence of mutants was determined mainly by the high percentage of embryonic lethal mutants, which is indicative of nonoptimum conditions for raising plants, since the incidence of mutants can rise appreciably under unfavorable conditions [4]. However, the reliably greater genetic disturbances in the examined experimental plants is indicative of the contribution of flight factors to this effect.

It is known that embryo death in a seed before it germinates, as well as cotyledon death of seedlings is caused to a significant extent by massive invasion of meristem cells by large chromosome aberrations [2, 4]. Gamete sterility is related to induction of smaller aberrations, which persist for

several cell division cycles. Apparently, the cells with these aberrations are selected in meiosis [4]. Since the incidence of chromosome aberrations in C. capillaris cells is considered in the first mitosis, it reflects the sum of all aberrations accumulated in meristem cells, both at the time of seed germination and during inflight cell division.

Potential disturbances accumulated in embryonic cells were manifested when the seeds germinated, lowering their germination and viability of seedlings, mainly at the early stages of development [8]. Both recessive mutations represented by micro-aberrations and gene mutations are involved in the lethal effect. Upon subsequent development of offspring of the "space" plants, the cells with chromosome aberrations were eliminated. This was indicated by the identical fertility of offspring of control and experimental plants in the Phyton-3 experiment. Micro-aberrations and gene mutations were also partially eliminated, as indicated by the lesser difference between experiment and control in number of recessive mutants in seeds of "space" plants and their offspring. However, this elimination was far from complete. Differences between the experiment and control with respect to mutability persisted on a statistically reliable level. Consequently, the changes related to micro-aberrations and gene mutations persisted at least for the next postflight generation. This is indicative of the sensitivity of the genetic test, which demonstrated postflight changes in offspring of experimental plants, whereas other methods (morphological and physiological) did not record any deviations from the control whatsoever [8].

Thus, it can be concluded that spaceflight factors have a mutagenic effect on plant cells, eliciting both structural chromosome aberrations and gene mutations in them. Developing systems are more sensitive to these factors than air-dried seeds. Structural mutations manifested in the plants themselves or at the early stages of development of their offspring are eliminated in the next generation. Point mutations persist after flight at least in part in plant offspring.

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T AND B COMPONENTS OF IMMUNITY IN THE PRESENCE OF ACUTE MOUNTAIN SICKNESS

[Article by M. M. Mirrakhimov, M. I. Kitayev, R. O. Khamzamulin,
A. G. Tokhtabayev and S. M. Pogrebitskiy]

[English abstract from source] Immunological aspects of the
adaptation process were investigated in 57 male test sub-
jects that stayed for 30 days at an altitude of 3600 m above
sea level (Eastern Pamir Mountain Range). The uneventful
development of adaptation was accompanied by a short-term
decrease in the number and activity of T-lymphocytes. An
acute mountain disease led to a distinct deficiency of T-cell
immunity which still persisted on test day 30. Besides, the
content of zero cells in circulating blood was increased and
the blast-transformation reaction of lymphocytes to concavalin A
was inhibited. Prior to the ascent the test subjects who were
susceptible to the acute mountain disease showed a lower content
of T-lymphocytes and a higher content of zero cells in
circulating blood.

[Text] Acute mountain sickness (AMS) is one of the most frequent deadaptation
complications observed when people spend a brief time at altitudes in excess
of 2.5-3 km above sea level [4]. Data have been accumulated about the inci-
dence [13] and clinical manifestations [3, 14] of AMS; methods have been
proposed for treatment [12, 19] and prevention [9] of this disease. However,
the question of condition of the different functional systems, including the
immunocompetent system, in the presence of AMS have been little-studied. More-
over, the distinctions of physiology and pathology of the latter system in
the mountains are among the least developed chapters of altitude medicine.
Previous studies have shown that man's adaptation to high altitude is charac-
terized by phasic changes in proportion and functional activity of T- and B-
lymphocytes [2].

Our objective here was to investigate T and B elements of immunity in victims
of AMS and possible immunological factors in essentially healthy individuals
favoring development of this sickness.

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METHODS

We conducted a clinical and immunological observation of 57 essentially healthy men during 3-day adaptation to an altitude of 3600 m above sea level (Murgab, eastern Pamirs). The subjects were divided into two groups, according to nature of the adaptation process. The 1st group consisted of 25 men with uneventful course of adaptation and the 2d, the remaining 32 subjects who developed AMS in a mild or moderately severe form within the first 3 days after the ascent.

The diagnosis of AMS was made on the basis of typical clinical signs (headache, vertigo, tinnitus, marked dyspnea and palpitations during exercise or at rest, bleeding, marked diffuse cyanosis, accented second sound over the pulmonary artery). It should be noted that the diagnosis of AMS was considered reliable when the above-listed symptoms persisted for at least 3-5 days.

All of the subjects submitted to immunological examination before the ascent, in the village of Gulcha (1650 m above sea level), then on the 3d and 30th days of adaptation to 3600 m above sea level. It included differentiated analysis of T and B elements of immunity.

T and B populations of lymphocytes in peripheral blood were tested and their function assessed with consideration of the recommendations of WHO experts. We used lymphocytes isolated from peripheral blood in a ficoll and urotrast gradient to identify and make a quantitative assay of T- and B-cells. T-lymphocytes were demonstrated by the method of spontaneous rosette formation with ram erythrocytes [15], B-lymphocytes were determined by their capacity to form rosettes with bovine erythrocytes loaded with M antibodies and the third component of complement [18]. We assessed the functional state of T-lymphocytes on the basis of the lymphocytes' blast-transformation reaction with phyto-hemagglutinin (PHA) and concanavalin A (Con'A) and their spontaneous blast transformation [7]. Functional evaluation of B-lymphocytes was made according to blood immunoglobulin A, M and G levels, which were measured by the method of radial immunodiffusion [16]. We counted null cells [11].

Results and Discussion

Examination of the subjects' immune status revealed that, even with a good course of adaptation, on the first days of the ascent to high altitude there was a decrease in number of rosette-forming T-cells (T-rfc) in blood and in their capacity to be transformed into blasts under the effect of PHA (see Table). By the 30th day of adaptation, the absolute number and functional activity of these cells were restored to baseline values.

In the course of our investigation, it was established that the reaction of blast transformation of lymphocytes with Con'A did not change appreciably in the mountains with an uneventful course of adaptation, which could be related to the effect of this mitogen on the subpopulation of T-cells, which manifest resistance to low oxygen pressure. At the same time, these subjects showed a substantial decrease in spontaneous lymphocyte transformation at high altitude.

T element of immunity in healthy subjects and those with AMS during adaptation to high altitude (M±m)

| Parameter | Baseline (1650 m above sea level) | | Day of adaptation to 3600 m altitude | | | |
| | | | 3 | 3 | 30 | 30 |
	healthy	AMS	healthy	AMS	healthy	AMS
T-rfc:						
%	68,7±3,1	60,1±1,1·	58,3±2,2*	52,6±1,7*·	68,4±4,1	54,1±3,2*·
absolute/µℓ blood	1210,0±44,2	1118,4±71,3	1020,5±36,3*	742,4±39,6*·	1247,0±66,4	912,2±56,6*·
PHA-stimulated cells,%	70,3±1,4	74,6±3,3	62,6±1,6*	56,9±2,2*·	70,5±2,3	59,4±3,1*·
Con'A-stimulated cells, %	68,4±2,6	70,8±5,4	67,1±4,3	56,6±4,9*	75,3±2,8	54,8±6,2*·
Spontaneous blast transformation of lymphocytes	7,4±0,3	7,2±0,4	4,0±0,2*	3,4±0,5*	4,5±2*	4,3±0,5*

Note: Dots refer to differences between parameters of healthy subjects and those with AMS ($P < 0.05$); asterisks indicate differences as compared to baseline data ($P < 0.05$).

As for the rosette-forming B cells, their percentage increased on the first days of adaptation (19.2±1.4%, versus 13.5±1.0%), but the absolute difference was unreliable (336.0±25.7 and 320.0±18.0; $P > 0.05$). There was no appreciable change in levels of immunoglobulins A, M and G in the systemic circulation, which reflects functional activity of B cells, in the early stages of adaptation, but by the 30th day there was intensification of immunoglobulin M synthesis (275.4±17.9, versus 187.7±20.2 IU/mℓ) which, as we know, reflects an early immunological reaction to thymus-independent antigens [5].

The mechanism of onset of T immunological insufficiency under the extreme natural conditions at high altitude could be related to many factors and, first of all, "the hypoxic syndrome," with which hypoxia of lymphoid and macrophage elements appears. In the light of the known data concerning activation of the adrenals on the first days of adaptation to high altitude [6, 10, 17], it can be assumed that corticosteroids have an immunodepressive effect on immunogenetic processes. In particular, the fact that single injection to guinea pigs of hydrocortisone leads to transient T lymphopenia [8] is in favor of this thesis. Such changes are adaptive, and they correspond to the dynamics of immunity in experimental animals under stress [1].

The function of the T element of immunity was more affected with development of deadaptation pathology at high altitude (see Table). In subjects with AMS, there was also a statistically reliable decrease in T-rfc in the systemic circulation and in their capacity for blast transformation under the effect of PHA, as compared to base data ($P < 0.05$), on the first few days at an altitude of 3600 m above sea level. However, these cells suffered functionally more than in subjects with uneventful adaptation. Thus, while blast transformation of lymphocytes with PHA decreased by 7.7% on the first days at high altitude in the 1st group of subjects, it decreased by 17.7% in the 2d group,

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i.e., by more than double. Moreover, the AMS subjects also presented a decline of the lymphocyte blast-transformation reaction under the effect of Con'A, the activity of which did not change appreciably in the control group.

All this indicates that, in the presence of AMS, there is a decline in functional activity of the subpopulations of T-lymphocytes that manifest resistance to this mitogen in subjects with uneventful adaptation.
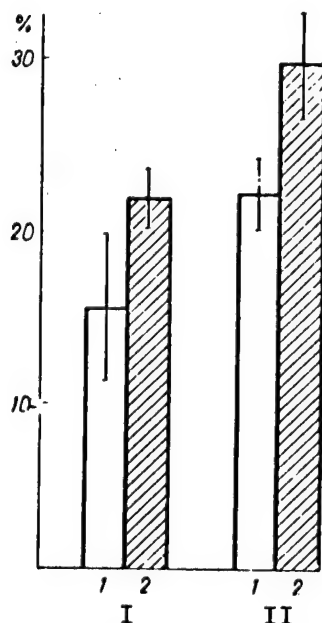
Null cells in essentially healthy subjects (1) and those with AMS (2)
I) baseline
II) 3d-5th day of adaptation

The T element of immunity remained depressed in the 2d group even 30 days after arriving at high altitude. The data listed in the table indicate that there was a drastic decrease in this group of subjects in quantity and functional activity of T-lymphocytes, not only at the intermediate (3d day), but last stage of the study (30th day).

Investigation of the B element of immunity in the presence of AMS is of definite interest, since we know that this element implements antibody synthesis.

The percentage of B lymphocytes in the systemic circulation did not change appreciably on the 3d day at high altitude in the 2d group of subjects, as compared to base data, unlike the 1st group, but it was lower than in healthy subjects who adapted to this altitude ($14.4\pm1.0\%$ versus $19.2\pm1.4\%$; $P<0.05$). B-lymphocyte content per unit blood volume (per $\mu\ell$) was the same in the 1st and 2d groups (336.0 ± 25.7 and 312.1 ± 17.0; $P>0.05$). However, these cells were functionally inadequate immuno-producers in the presence of AMS by the 30th day of adaptation, there was a drastic decline in level of immunoglobulins M, as compared to healthy subjects who adapted to the same conditions (144.1 ± 17.0 IU/mℓ, versus 275.4 ± 17.9 IU/mℓ; $P<0.05$). All this indicates that AMS also affects the B component of immunity.

The move to high altitude lead to increase in the systemic circulation of percentage and absolute number of null cells per unit blood volume. A more significant elevation of this parameter occurred with development of acute mountain sickness (see Figure). The opinion has been voiced in the literature that null cells are self-styled uncommited precursors of T-lymphocytes [5]. For this reason, one would think that an increase in number of null cells in essentially healthy people at high altitude and with AMS is perhaps related to their slower maturation when immunocompetent cells are not adequately supplied with oxygen; however, this matter requires special investigation.

Retrospective investigation of the distinctions of adaptation as a function of baseline immunological status in subjects suffering from AMS revealed a decrease, in the foothills (1650 m), in percentage of T-rfc in the systemic

circulation and in absolute null cell content. These data warrant the assumption that the decline of T-lymphocytes in the systemic circulation and increase in number of null cells have an adverse effect on adaptive changes at high altitudes.

The results of this investigation enable us to maintain that, in the presence of AMS, there is depression of the thymus-dependent element of immunity.

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EFFECT OF DIFFERENT DOSES OF ULTRAVIOLET RADIATION ON VITAMIN LEVELS IN MAN

[Article by M. S. Belakovskiy, M. G. Yuzhanskaya, N. Ye. Panferova, L. Kh.
Pastushkova, O. G. Pereverzeva, A. N. Smirnova, I. N. Sergeyev and
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[English abstract from source] Exposure of healthy adults
to prophylactic doses of UV-radiation in the medium and
long wavelength spectrum improved metabolism of vitamins A,
E and D and increased their content in the body. UV-ir-
radiation even in prophylactic doses increased ascorbic acid
requirements. Excessive UV-radiation produced an adverse
effect on the vitamin content. However, the vitamin concen-
tration in blood was not significantly decreased. This can
be explained by the adaptation of the human body to UV-irradia-
tion upon a continuous increase of its dosage.

[Text] Ultraviolet radiation (UVR) from the sun and artificial UVR have an
active effect on basic vital functions. UVR has a significant effect on
utilization and metabolism of vitamins in the body. The role of UVR in
photochemical synthesis of vitamin D in the skin is well-known. Many authors
believe that low doses enhance utilization of vitamins, while excessive UVR
intensifies their breakdown and elimination, thereby leading to vitamin de-
ficiency [3, 4, 10, 11]. It is known that some groups of people experience
prolonged UV deficiency by virtue of their distinctive working conditions or
place of residence, which makes it necessary to treat them with artificial
UVR. When using UVR preventively, it is important to take into consideration
the diversity of its effects on man. Our objective here was to investigate
the effects of different doses of UVR in the medium and long-wave range on
vitamin supply in healthy adults.

Methods

As a source of UVR we used fluorescent lamps emitting 0.97 W/m^2 in the wave-
length range from 280 to 400 nm. Before starting a course of UVR, we deter-
mined each subject's individual skin sensitivity to UVR on the basis of the
minimal erythemic dose (MED). We tested two groups of healthy adult men who
submitted to 20 sessions of UVR therapy for 40 days: the 1st group received
0.75 MED per treatment and the 2d, from 0.5 to 3 MED. After 10 treatments,

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total exposure time per subject constituted 112±7 min in the 1st group and 93±7 min in the 2d group; after 20 treatments, the corresponding times were 225±15 and 379±5 min, respectively. Throughout the period of our investigation, the subjects were on a controlled diet containing the recommended amount of vitamins in the form of 1 undevit [multiple vitamin] lozenge per day. In the baseline period, after 10 and 20 UVR treatments, as well as in the recovery period, we drew blood from the ulnar vein on a fasting stomach and assayed vitamins in serum: retinol, carotenoids, α-tocopherol, cobalamins, folic and ascorbic acids, 25-OH-D [1, 7, 12-14], as well as concentrations of calcium, phosphorus and activity of alkaline phosphatase [2]. We measured excretion of thiamin, riboflavin and N_1-methylnicotinamide in 24-h urine [5, 6, 15].

Results and Discussion

The results of the tests performed in the baseline period indicate that vitamin content did not exceed the physiological norm. We describe below the changes in vitamin content of blood serum in the course of the entire period of investigations (Figures 1 and 2, Tables 1 and 2).

Vitamin A and carotenoids. Serum vitamin A content after 10 UVR sessions increased by 51% (P<0.05) in the 1st grup and 34% (P<0.05) in the 2d. In the recovery period, the concentration of retinol in blood serum of the 1st group of subjects decreased, whereas in the 2d group it continued to increase. Carotenoid content increased insignificantly, by 19-24%, after 10 treatments, and in the recovery period it decreased to baseline values. Thus 0.75 MED UVR increased the serum concentrations of vitamin A and carotene, which could be due to their improved absorption in the small intestine or increased secretion of retinol-binding protein by the liver. The decrease in carotenoid concentration in the recovery period could be due to their more intensive conversion into retinol.

Ascorbic acid. After 10 UVR treatments, the concentration of reduced ascorbic acid increased unreliably by 23% in the 1st group and decreased by 20% in the 2d group of subjects. After 20 UVR treatments, ascorbic acid content in serum decreased by 14-19%. After 12-29 days, the concentration of vitamin C in blood fluctuated. UVR, even in preventive dosage, led to significant outlay of ascorbic acid (oxidation in the skin, UVR as an antioxidant). The decrease in blood concentration of ascorbic acid [10, 11] is indicative of a need to augment vitamin C content in the diet.

Vitamin E. After 10 UVR treatments, α-tocopherol content of serum increased by 29-32% (P<0.05). This is attributable, in the first place, to the fact that the high level of catecholamines with UVR enhances lipolysis, mobilization of lipids and free fatty acids from the lipid pool into plasma and corresponding migration of vitamin E into plasma; in the second place, to removal of tocopherol from cell membranes during hemolysis at the site of irradiation of the skin [9]. After 20 UVR treatments, α-tocopherol level in serum did not change in the 1st group of subjects. Evidently, this is related to the adaptation process. In the 2d group of subjects, whose irradiation time was increased, the serum α-tocopherol concentration decreased by 24% (P<0.05), as compared to the concentration after 10 UVR sessions, but was still above baseline values. Evidently, this is indicative of excessive UVR exposure of this group (breakdown of tocopherols by UVR and its utilization as an antioxidant).
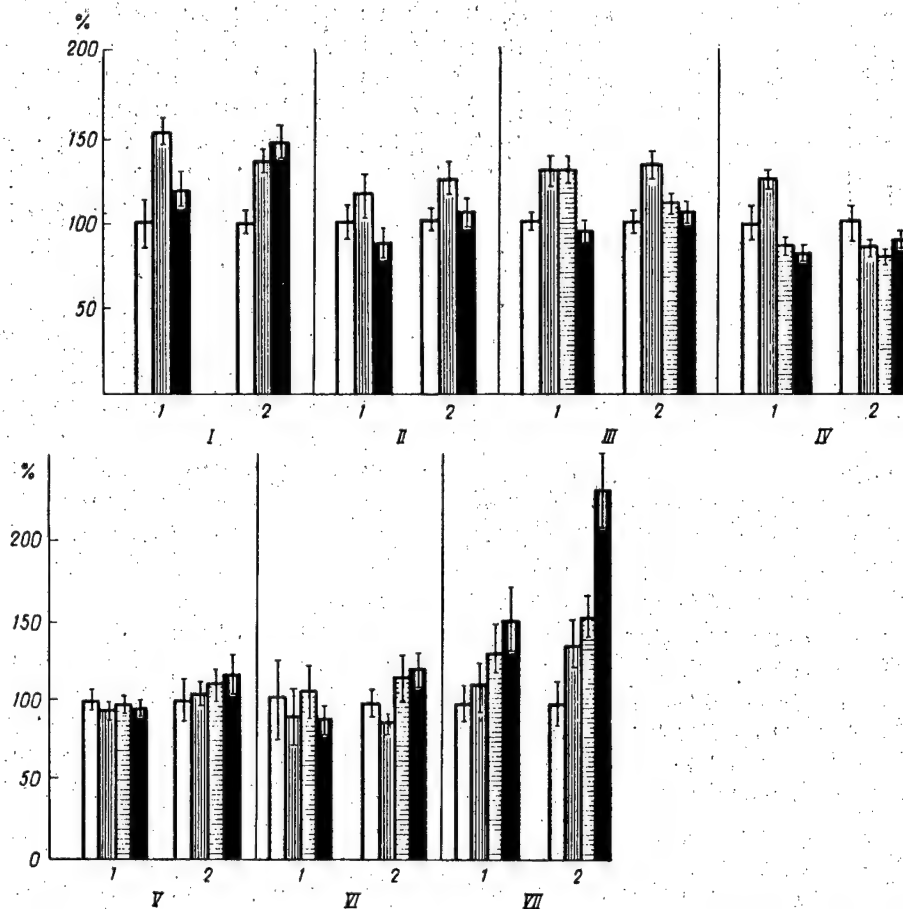
Figure 1.   Changes in blood serum vitamin levels after exposing subjects
to UVR (% of baseline)

  I) retinol
 II) carotenoids
III) α-tocopherol
 IV) ascorbic acid

V) cobalamins
VI) folic acid
VII) 25-OH-D

Here and in Figure 2:
 1, 2--1st and 2d groups of subjects respectively; white bars--baseline;
vertical and horizontal stripes--10 and 20 UVR treatments, respectively;
black bars--12 days after UVR

Vitamin B_{12} and folic acid.   During the studies, cobalamin and folic
acid concentrations were within the physiological range.   The subjects in the
2d group had a tendency toward increase in serum cobalamins and folic acid
during exposure to UVR.

Vitamin D.   Exposure of the skin to UVR leads to accumulation in it of
substances with antirickets activity.   This process depends on the intensity
of irradiation.   There are indications in the literature of "deferred" in-
crease in concentration of vitamin D metabolites after UVR [8].   In our
studies, the concentration of vitamin D metabolite (25-OH-D) in the 1st group
of subjects increased by 14% (P<0.05) after 10 treatments, by 34% after 20
(P<0.05) and by 54% 12 days after UVR (P<0.05), as compared to the baseline.

Table 1. Blood vitamin levels before and after UVR (M±m)

Group	Time of examination	A, μg/100 ml	Carotenoid, μg/100 ml	C, mg/100ml	E, mg/100ml	B_{12}, pg/ml	Folic acid, ng/ml	25-OH-D, ng/ml	Ca, mg/100 ml	Pi, mg/100 ml	Alkaline phosphatase, mU/ml
1	Baseline	63,30±23,97	108,60±23,18	1,26±0,32	0,99±0,12	724±98	5,90±3,20	42,30±9,60	9,9±0,4	4,1±0,2	50,9±3,1
	After 10 UVR treatments	94,90±9,38	128,00±30,89	1,55±0,06	1,28±0,18	671±95	5,20±1,90	48,70±12,00	10,3±0,1	4,5±0,2	50,4±5,4
	After 20 "	—	—	1,08±0,05	1,29±0,11	708±83	6,20±2,30	57,00±13,7	10,3±0,2	4,7±0,1	50,7±5,4
	Recovery period(RP)	75,10±16,37	93,10±26,61	1,05±0,10	0,90±0,08	703±87	5,20±0,82	65,30±13,00	9,9±0,5	5,4±0,6	49,9±4,4
2	Baseline	55,7±7,64	149,60±20,89	1,29±0,33	1,11±0,16	562±175	4,4±0,56	32,70±8,20	9,7±0,3	4,5±0,6	49,7±2,2
	After 10 UVR	74,70±4,79	185,80±31,75	1,05±0,13	1,46±0,17	585±80	3,8±0,30	45,70±10,60	10,2±0,3	4,7±0,4	50,2±3,9
	After 20 UVR	—	—	1,04±0,4	1,20±0,14	620±134	5,2±1,10	51,00±10,00	10,3±0,3	4,6±0,5	48,3±4,0
	RP	82,20±10,27	156,10±38,29	1,12±0,10	1,16±0,09	663±126	5,3±0,33	77,30±15,80	10,4±0,4	5,3±0,8	51,3±1,3
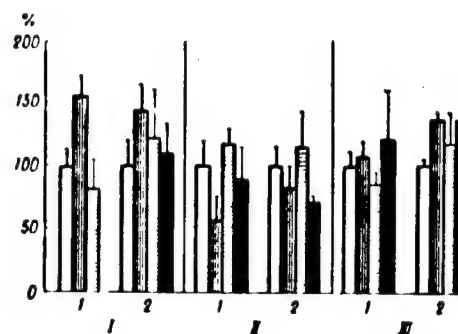
Figure 2.
Change in daily excretion of vitamins
in urine with UVR (% of baseline)
  I) thiamine
  II) riboflavin
  III) N_1-methylnicotinamide

The rate of vitamin D production in
this group is directly related to
exposure time. The significant in-
crease in concentration of active
metabolite of vitamin D is indicative
of active photochemical synthesis of
vitamin D from provitamin (7-dehydro-
cholesterol) in the skin under the
effect of UVR, its active absorption
into the intestine and blood, and
intensive production of 25-OH-D in the
liver. In the 2d group of subjects,
serum 25-OH-D concentration increased
by 56% (P<0.05) after 10 UVR treat-
ments and by 136% (P<0.05) 12 days
after UVR. A comparison of the rate
of increase in blood 25-OH-D concentra-
tion in both groups after 10 UVR treat-
ments shows that it is 2.8 times
greater in the 2d group (P<0.05). Let
us mention that mean total irradiation
time is about the same in the 2 groups
after 10 UVR treatments. The dosage of
UVR per session increased by the 10th
treatment from 0.5 to 1.7 MED in the
2d group, i.e., the 2d group of sub-
jects received 2.4 times MED by the
10th session than the 1st group. Thus,
the rate of vitamin D synthesis with
the same optimum duration of UVR is
inversely proportionate to MED level.
After the 20th UVR treatment, blood
serum 24-OH-D concentration increased
1.6 times more in the 2d group than in

the 1st, and mean total irradiation time after the second 10 treatments was twice as long than in the 1st group, while UVR in MED per treatment was 4 times higher than in the 1st group. We observed slower synthesis of 25-OH-D which was related to exposure to excessive dosage of UVR, as well as development of processes of adaptation to UVR. The increase in vitamin D supply during UVR was associated with some increase in concentrations of Ca and Pi in blood serum, which could be attributed to intensification of vitamin D-dependent processes of absorption of these elements in the intestine [8].

Table 2. Daily excretion of vitamins and their metabolites in urine of subjects (3 individuals) with different doses of UVR (M±m)

Time of examination	First group			Second group		
	B_1, µg	B_2, µg	PP, mg	B_1, µg	B_2, µg	PP, mg
Baseline	593,3±92,6	528,8±116,7	7,37±1,03	550,0±114,0	585,2±101,7	6,77±0,17
After 10 UVR	911,0±92,1	288,8±100,9	7,90±0,89	792,2±114,1	477,4±89,0	9,37±0,17
After 20 UVR	489,0±159,0	619,6±57,1	6,53±0,65	667,8±194,5	668,0±193,2	8,00±1,64
Recovery period	—	475,2±34,0	9,05±3,6	611,8±119,6	426,8±13,5	9,30±1,78

Analysis of daily excretion of vitamins in urine revealed increased discharge of thiamine after 10 UVR treatments--44-54% (P<0.05). After the 20th treatment, thiamine excretion remained somewhat high in the 2d group of subjects. This is apparently attributable to intensification of function of thiamine-dependent enzymes of carbohydrate and lipid metabolism. Elimination of riboflavin in urine after the 10th treatment decreased by 18-45%. After 20 UVR sessions, there was a 14-17% increase in excretion of vitamin B_2 in urine, which is indicative of excessive exposure of subjects to UV rays [5, 6]. There was rapid recovery.

Vitamin PP. While only insignificant changes were demonstrated in the 1st group of subjects with regard to excretion in urine of N_1-methylnicotinamide, and they were in different directions, in the 2d group excretion of this vitamin increased by 38% already after the 10th treatment (P<0.05). Active elimination of the vitamin PP metabolite in urine has been described in the literature as a test for excessive UVR [3, 5].

To sum up the results of our study of vitamin metabolism with exposure to UVR in the medium and long-wave range of the spectrum, it is apparent that in this mode of UVR optimization of metabolism of all vitamins is proportionate to UVR exposure time (optimum amount of UVR) and it is unrelated to MED. This hypothesis is confirmed by the fact that no reliable differences were demonstrated in vitamin metabolism between the 1st and 2d groups of subjects after 10 sessions of UVR. Overall UVR exposure time was about the same in the groups, whereas there was a 2-fold difference in MED received per treatment by the end of the 10th one. The increase in concentrations of vitamins A, E and D is indicative of the stimulating effect of UVR. The decrease in blood ascorbic acid concentration and the increased ascorbic acid requirement with

exposure to UVR, which is reported in the literature, justifies our suggestion to increase vitamin C content in the diet of individuals exposed to UVR. Preventive UVR leads to significant increase in endogenous vitamin D, the rate of production of which is directly related to UV exposure time and MED per treatment. We consider the optimum to be the conditions of receiving UVR by the 1st and 2d groups of subjects after 10 treatments. After 20 UVR treatments, we did not observe further increase in vitamin content (with the exception of vitamin D) of blood in both groups. The differences in concentrations of vitamins in the two groups are also unreliable. This can be attributed to some UVR overdose after 20 treatments. The increase in excretion of riboflavin and N_1-methylnicotinamide in 24-h urine, as well as the fact that vitamin A and D levels were slightly above the top of the physiological range after 20 UVR sessions in the 2d group, are indicative of excessive UVR. However, in this case we failed to observe a significant decrease in concentration of vitamins in blood. This is attributable to the mechanism of adaptation to UVR with gradual increase in its dosage, as described in the literature.

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PHYSICAL ENDURANCE OF RATS DURING INTENSIVE AND REPEATED EXPOSURE TO
STATIONARY MAGNETIC FIELD

[Article by L. V. Kokoreva]

[English abstract from source] Variations in physical
endurance of rats exposed to a constant magnetic field of
1.6 T for 3 hours a day during 30 days were investigated.
The parameter was measured as the time of swimming with a
load making 10% of body weight until complete arrest. The
rats exposed once, 5 or 15 times showed a longer time of
swimming than the controls. On the 30th day of exposure there
was no difference between the experimental and control animals.
The data obtained suggest that exposure to a constant magnetic
field produces a stimulating effect on physical work capacity
during the first 15 days.

[Text] There are fragmentary and contradictory experimental data concerning
the effect of stationary magnetic fields (SMF) on physical endurance and work
capacity. It was established that 5-fold exposure to SMF with induction of
0.007 T for 10 h/day shortened significantly maximum swimming time in mice
[1]. This led to the conclusion that physical endurance of animals diminishes
under the effect of SMF. Different results were obtained with one-time use
of stronger magnetic fields. Thus, it was found that SMF of 0.05 (1 h) and
0.1 T (1 and 24 h) did not change work capacity of mice, while induction of
0.4 T (1 h) noticeably enhanced it, as assessed by the swimming method [6, 9].
An increase in static work capacity of rats (longer time of staying on a bar)
was demonstrated after 4-5-h exposure to SMF of 0.3 T [9]. Along with these
data, there are reports of absence of effect of exposure to SMF with induction
of 1.6 T for 3-4 h on static work capacity of rats [9] or of 2-month con-
tinuous exposure to a drastically heterogeneous SMF with maximum induction
of 0.15 T on dynamic work capacity (swimming method) of mice [2].

Our objective here was to investigate the dynamics of changes in physical
endurance of rats in the course of month-long exposure to divided doses of
SMF with induction of 1.6 T.

Methods

We conducted this study on 58 male mongrel rats. Experimental animals were submitted to total body exposure to a vertical magnetic field with induction of 1.6 T for 3 h daily. We used an SP-57A electromagnet with polar tips in the form of a circle 900 mm in diameter and air gap of 100 mm between them to generate the magnetic field. The latter was strictly stationary and homogeneous in a radius of 380 mm, and toward the edge of the pole tip induction dropped to 1.3 T. The rats were placed in the gap of the electromagnet in plexiglas cages in the shape of a circle sector. Control animals were kept in the same room under analogous conditions in a phantom of the polar tips made of duralumin. All of the animals received a complete food allowance in the form of mixed feed and water at lib. Work capacity of the rats was evaluated on the basis of swimming time with a weight that constituted 10% of the animal's body weight, until all motor activity stopped. Water temperature in the tank was 32°C. The test was performed individually on each animal at a strictly specific time of day. To rule out the possibility of a conditioning effect, experimental and control rats swam once on the 1st, 6th, 15th and 30th days of exposure to SMF, and the experimental ones also swam right after termination of 3-h exposure.

Results and Discussion

Observation of the general condition of rats submitted to 3-h SMF of 1.6 T daily failed to reveal differences from control animals. The experimental and control groups of animals were equally active, had clean shiny fur and consumed their feed willingly. Baseline weight was the same in the control and experimental groups (180-190 g); however, the experimental animals gained weight somewhat more intensively, particularly in the first 2 weeks of the experiment. On the 15th day of exposure the differences between the experiment and control were statistically reliable. Thereafter, they diminished significantly. There was little difference between the weight of rats submitted to SMF of 1.6 T 30 times and control rats (256.65 ± 6.7 and 247.5 ± 7.73, respectively).
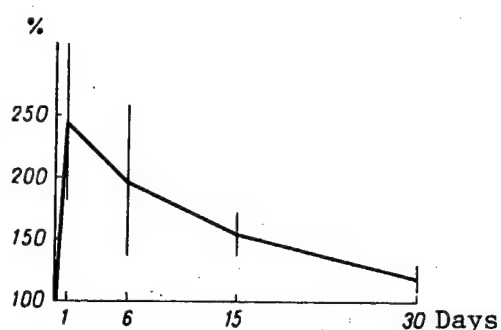
Physical endurance of rats during exposure to divided doses of SMF of 1.6 T for 30 days
  X-axis, days of exposure to SMF;
  y-axis, maximum swimming time
  (% of control)

The results of the swimming test revealed that the effect of SMF on physical endurance of rats depended appreciably on the frequency of exposure to SMF.

In control rats, maximum swimming time held at a stable level for 1 month. At the start of the experiment it constituted 2.71 ± 0.44 min and after 30 days, 2.77 ± 0.33. After single 3-h exposure to SMF of 1.6 T, maximum swimming time was more than twice as long as in the control and constituted 6.59 ± 1.66 min ($P < 0.05$). These findings agree with the results of studies, in which it was shown that single exposure to high-intensity SMF can enhance physical work capacity of animals [6, 9]. The greatest effect was demonstrated after single

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exposure. After repeating exposure to SMF for 5 and 15 times, swimming time remained considerably longer than in the control, whereas by the 30th day it decreased to virtually the control level (see Figure).

Thus, repeated exposure to SMF of 1.6 T for 3 h per day enhances physical endurance of rats for the first 15 days and retards considerably development of fatigue. We failed to observe a cumulative effect of the magnetic field. Conversely, upon repeated exposure to SMF for a longer period, the effect is attenuated and is no longer demonstrable after 30 exposures. The mechanisms at the basis of the stimulating effect of SMF on work capacity require special analysis. It is opportune to mention that SMF elicits a reaction by the sympathoadrenal system [3, 4]. Its effect on physical endurance is well-known [7, 8]. We previously demonstrated that activation of the sympatho-adrenal system is the most significant on the first 12 days, whereas by the 30th day the extent of increase in blood catecholamine concentrations diminishes and no reliable differences from the control are demonstrable [5]. These data suggest that an increase in function of the sympathoadrenal system plays a substantial role in expression of the stimulating effect of SMF on work capacity Nor can we rule out the possibility that SMF also affects a number of other physiological systems.

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RADIOBIOLOGICAL VALIDATION OF QUALITY FACTOR OF PROTONS AND HELIUM IONS

[Article by N. I. Ryzhov and B. S. Fedorenko]

[English abstract from source] Reported data and experimental
results of measuring the relative biological effectiveness of
protons of different energies and helium ions of 4 GeV/nuclon
were analyzed to determine quality factors of the major com-
ponents of cosmic radiations. It is recommended to use
quality factors equal to 1.30-1.45 for 100-730 MeV protons and
equal to 1.75 for 9 GeV protons and 4 GeV/nuclon helium ions.
It is also suggested to employ them as standards for solving
practical problems of radiation safety in spaceflights.

[Text] Analysis of the literature and results of investigating biological
activity of proton over a broad spectrum of energy and helium ions warrants
the belief that recommendations can be submitted on their basis for
quality factors (QF) of protons and helium ions as applied to problems of
assuring radiation safety of spaceflights.

As we know, up to 1962, data concerning relative biological effectiveness
(RBE) of radiation, to which personnel could be exposed when performing
certain professional measures, were used to set standards for radiation
levels and designing work related to planning protection against ionizing
radiation. However, in view of the variability of coefficients of RBE of
radiation and their dependence on concomitant effects of other factors, diffi-
culties often arose in selecting concrete RBE factors to solve specific
practical problems. In accordance with the recommendations of the Committee
for RBE under the International Commission for Radiation Protection, it was
proposed to use the QF of radiations to perform the above-mentioned work [12].
The latter is a dimensionless parameter determining the adverse biological
consequences of exposing man to low doses of radiation as a function of com-
plete linear energy transfer (LET) of radiation [6]. Standard QF are based
on coefficients of RBE of radiation and their dependence on LET obtained in
experimental investigations and extrapolated to the range of low doses and
chronic exposure.

At the present time, the QF values for protons listed in Table 1 are used in the USSR in design and planning work dealing with protection against ionizing radiation and setting the range of doses [1, 6], as well as in the practice of assuring radiation safety of spaceflights [3].

Table 1.
Stipulated QF and RBE coefficients of protons [1, 6]

Proton energy, MeV	QF	RBE coefficient
10	9,4	2,2
20	7,0	1,3
50	4,7	1,0
100	3,4	1,0
200	2,4	1,0
500	2,1	1,0
1000	2,1	1,0

As can be seen in Table 1, there are considerable differences in RBE coefficients and quality factor of proton radiation on the same energy level. In the presence of such differences, the logical question arises as to the validity of using the stipulated values for coefficients of the proton quality factor indicated in the table to assure radiation safety of spaceflights.

In the case of relatively short flights when there is low probability of acute irradiation of cosmonauts, use of the standard QF for protons can be acceptable on the whole, although without sufficient justification. However, in the case of long-term missions, when there is a possibility of exposure to radiation in doses considerably higher than the standard level [3], use of the QF listed in Table 1 could lead to unwarranted exaggeration of the mass of protection and underestimation of the payload mass. In this regard, we should recall that, according to [6], use of QF in the range of stipulated values is allowed only when there is a possibility of exposure to radiation in an overal equivalent dose not exceeding 5 maximum allowable doses (MAD), i.e., 25 rem. Yet, according to [3], the standard radiation levels are 50 to 150 rem for spaceflights lasting 1 to 12 months. Single exposure to radiation during spaceflights is limited to 50 rem. Consequently, the standard QF listed in [6] cannot be used entirely in practical assurance of radiation safety of spaceflights. These circumstances served as grounds to conduct the present study, the purpose of which was to validate experimental data on QF of the principal components of cosmic radiation--protons and ions of helium--for use in practical implementation of radiation safety of spaceflights.

The proposed values for proton QF are based on experimental values of proton RBE coefficients, which adequately reflect the biological effectiveness of protons with reference to standard radiation in the dose range regulated [3] by criteria of early and long-term somatic and somatostochastic consequences of irradiation (with the exception of genetic effects) [2, 4].

Calculation of equivalent dose referable to chronic exposure to protons was made on the basis of the recommendations in [6]. Mean values of proton RBE coefficients on different energy levels were determined on the basis of consideration and averaging of the values of the corresponding coefficients obtained on large mammals and biological material taken from man [1, 2, 4, 7, 10, 11].

Proceeding from the basic principle of providing radiation safety and "not to exceed the established basic dose limit" [6], in determining proton QF we

considered that these proton QF must not be below the top values of confidence limits of proton RBE coefficients of the corresponding energy level. We determined the confidence limits of proton RBE with a probability (0.01) exceeding that of the other protection systems.

The standard proton QF that we developed are proposed for use exclusively on assuring radiation safety of spaceflights lasting up to 1 year in cases where acute single exposure to radiation do not exceed 0.5 Gy and repeated doses do not exceed 1.5 Gy in the course of a year.

In accordance with the above-described principles and approaches, we processed the available data on biological effectiveness of protons and determined the mean RBE coefficients of this radiation with confidence limits for monkeys and dogs, as well as material taken from man. The results of this processing are listed in Table 2.

Table 2.
Mean proton RBE coefficients on different energy levels

Material	Proton energy, MeV		
	100—240	250—490	500—730
Monkeys	1,00±0,10	1,00±0,10	1,15±0,10
Dogs	1,00±0,10	1,04±0,10	1,07±0,10
Human tissue and cells	0,95±0,10	—	0,98±0,04
Mean RBE	0,98±0,13	1,02±0,12	1,07±0,13

Table 3.
QF for protons on different energy levels

Proton energy, MeV	Mean RBE coefficient	RBE coefficient on top boundary of confid interval (P=0.01)	QF
100—240	0,98±0,12	1,32	1,30
250—490	1,02±0,12	1,36	1,35
500—730	1,07±0,13	1,44	1,45

Table 3 lists the recommended QF for protons on different energy levels. They were obtained by rounding the values for the top confidence limits of proton RBE coefficients.

Applying the above principles and approaches, we provided a radiobiological validation of QF for protons with energy of 9 GeV and helium ions with energy of 4 GeV/nucleon. The biological material was exposed to protons (0.25-4 Gy) and helium ions (0.25-6 Gy). We tested radiobiological effects as a function of type of material 12 h to 30 days after exposure to radiation. We used ^{60}Co γ-radiation as standard radiation. Analysis of the results of the tests with protons and helium ions with energy of 9 GeV and 4 GeV/nucleon, respectively, revealed that when biological material was exposed to them there was development of radiation lesions which did not differ qualitatively from those induced by standard radiation. As for quantitative assessment of effects, according to most parameters, at the early postradiation stages (up to 30 days) both protons and helium ions had a more marked biological effect. The RBE coefficients of protons and helium ions were in the range of 1.0-2.7 (Table 4). Mean RBE coefficients for these radiations are 1.5±0.1.

Thus, the data on RBE of protons and helium ions indicate that these radiations are, on the average, 1.5 times more effective than standard forms of radiation. Since these results were obtained on the basis of averaging the parameters of

the general reaction of the animals' entire body, its critical systems and organs (marrow, gonads), it can be considered that they objectively reflect the corresponding relationships in biological effectiveness of the radiations in question. Moreover, since these data are quite consistent with parameters obtained from studies of human lymphocytes, it can be considered that the above-mentioned mean RBE coefficients of protons of 9 GeV and helium ions with energy of 4 GeV/nucleon can be also used for quantitative evaluation of reactions of the whole human body to radiation. This justifies our recommending the established coefficients of RBE of the radiations in question as temporary standards.

Table 4. RBE coefficients of 9 GeV protons and 4 GeV/nucleon ions

Material	Tested effect	RBE coefficient		Reference
		protons	He ions	
Mice	Mortality rate	—	1,4	[9]
Mouse bone marrow	Incidence of aberrant cells	2,0±0,3	2,0±0,5	[4]
	Number of karyocytes	1,5±0,3	—	
	Proliferative activity	—	1,6±0,1	
Mouse corneal epithelium	Incidence of aberrant cells	1,9±0,2	2,7±0,3	[2,4]
	Proliferative activity	1,6±0,5	1,6±0,5	[8]
Mouse epidermis	Incidence of aberrant cells	1,0	1,0	
Mouse testes	Type A spermatogonia survival	1,2	1,0	[5]
	Type B spermatogonia survival	1,7	1,2	
Human lympho-cyte culture	Incidence of aberrant cells	1,4±0,2	1,6±0,2	[4]
	Overall incidence of chromosome aberrations	1,6±0,2	1,6±0,2	
Chinese hamster cells	Incidence of aberrant cells	—	1,3±0,1	[4]
	Overall incidence of chromosome aberrations	—	1,2±0,1	
RBE coefficient		1,5±0,1	1,5±0,1	

Note: Dashes signify that no data are available.

The obtained RBE coefficients for high-energy protons and helium ions were used to validate the QF of these forms of radiation. And, proceeding from the above principles of radiation safety, it was considered that QF must not be lower than the top of the confidence limits of mean RBE coefficients. The reliability of confidence limits was taken with a probability of 0.05, which satisfied the principal requirements and reliability of the established QF of radiations.

In accordance with the above-described requirements, QF constituted 1.75 for protons of 9 GeV and helium ions with energy of 4 GeV/nucleon. Since the QF were determined in accordance with the basic standard-related documentation [3, 6], recommendations of the International Commission for Radiation Safety [7] and the results of radiobiological studies of immediate effects of radiation, but without consideration of long-term and remote sequelae [2, 4], we can consider the submitted data as temporary standards for QF, which can be

used to solve problems of assuring radiation safety of spaceflights. In view of the foregoing, it is recommended to consider QF of 1.30-1.45 for protons in the energy range of 100 to 730 MeV. These values are recommended for determination of allowable levels of exposure of man to radiation and calculation of protection against it in cases of acute and repeated exposure. QF should be considered to be 1.75 for protons with energy of 9 GeV and helium ions with energy of 4 GeV/nucleon.

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EFFECT OF DIBASOL AND SOME OF ITS IMIDAZO ANALOGUES ON ANIMAL TOLERANCE TO GRAVITATIONAL ACCELERATIONS AND DYNAMICS OF DEVELOPMENT OF POSTISCHEMIC CEREBROVASCULAR PHENOMENA

[Article by V. K. Vereshchagin and M. D. Gayevyy]

[English abstract from source] Anesthetized and nonanesthetized animals (white rats and cats) were used to study the effect of dibazolum and its new imidazo analogs (designated AKS-67 and AKS-87) on animal tolerance to gravitational effects and cerebral ischemia (ligation of both carotid arteries), as well as on systemic arterial pressure and tone of cerebral and peripheral vessels (resistographically) in the postischemic period. The drugs were administered 30-90 min before exposure. It was found that in nonanesthetized rats dibazolum and AKS-87 increased tolerance to cranio-caudal acceleration and decreased it to caudo-cranial acceleration, whereas AKS-67 produced a distinct protective effect regardless of the vector. In anesthetized rats (bilateral carotid ligation) AKS-67 and AKS-87 increased acceleration tolerance and dibazolum produced no protective effect. Dibazolum enhanced postischemic hypotension while AKS-67 and AKS-87 delayed or completely arrested it. For aerospace medicine the drug AKS-67 is of particular importance because it increases significantly animal tolerance to acceleration and stabilizes arterial pressure in the postischemic period.

[Text] Impairment of regional circulation, particularly in the brain, is one of the main pathogenetic elements in the effect of FGz gravitational accelerations. The latter require some strain of adaptive adjustments [11]. It is also known that typical cerebrovascular syndromes appear in the post-ischemia period: excessive perfusion and hypoperfusion [3, 4, 12, 19, 20]. A number of authors [1, 2, 16, 18] have reported the beneficial effect of di-basol on cerebral circulation and enhancement of the body's resistance to various exogenous adverse factors that elicit hypoxia [8-10, 14], including gravitational loads [15, 17] and motion sickness [7].

Investigation of some new derivatives of imidazobenzimidazole [6, 13] revealed that they have more activity than dibasol. Our objective here was to make a comparative study of the effect of dibasol and some of its new analogues (laboratory codes AKS-67 and AKS-87) furnished by Professor G. V. Kovalev on constitutional tolerance to circulatory hypoxia of the brain (gravitational loads, ligation of both common carotid arteries) and dynamics of development of postischemia cerebrovascular phenomena.

Methods

We tested tolerance to gravitational loads on 108 unanesthetized white rats of both sexes weighing 200-220 g on a centrifuge 2 m in diameter, with consideration of previous recommendations [5]. We selected the level of gravitational accelerations so as to have animal mortality in the control group close to 50%. In the experiments, we used craniocaudal (18 G for 10 min) and caudocranial (5-7 G for 5 min) vectors of acceleration.

Both common carotid arteries were ligated in 63 white rats of both sexes weighing 160-250 g anesthetized with sodium pentobarbital (20-30 mg/kg). The drugs were injected intraperitoneally 30-90 min before exposure or ligation of vessels in a dosage of 2-3 mg/kg (1 ml/kg 0.2-0.3% solution). In control tests, the rats were given intraperitoneal injections of saline in the same volume. The dynamics of development of postischemic cerebrovascular phenomena during perfusion of vessels with a stable volume of blood were studied on 33 cats of both sexes weighing 2.6-4.3 kg using a previously described method [3]. Cats, which were anesthetized with 40-50 mg/kg sodium pentobarbital, were given intravenous injections of the tested agents in a dosage of 2-3 mg/kg 90 min before ischemia. Systemic arterial pressure (SBP) and perfusion pressure (PP) were recorded using mechanotrons (6-MDZh-11-S) on an N-338 automatic recorder.

Results and Discussion

In the control experiments, 12 out of 27 animals survived (55.6% mortality) gravitational accelerations in a caudocranial direction and 9 out of 18 (50% mortality) survived among those submitted to craniocaudal accelerations. Preventive administration of dibasol enhanced animal resistance to gravitational accelerations in a craniocaudal direction, as indicated by the 1.8-fold increase in number of surviving animals (11 out of 12 survived), as compared to the control. With change in vector of acceleration (caudocranial) the number of survivals decreased by 25%, as compared to the control (Figure 1a, b). Preadministration of AKS-67 increased the survival rate in the case of both craniocaudal (10 out 12 animals survived) and caudocranial (8 out of 9 survived) direction of gravitational accelerations, as compared to the control. With use of AKS-87, animal survival rate increased 1.5-fold with craniocaudal gravitational accelerations (9 out of 12 animals survived), as compared to the control. However, with change in acceleration vector (caudocranial direction), there was a 25% decrease in surviving animals, as compared to the control.

Thus, dibasol and AKS-87 (to a lesser extent) enhanced rat resistance to gravitational accelerations in a craniocaudal direction, lowering it with
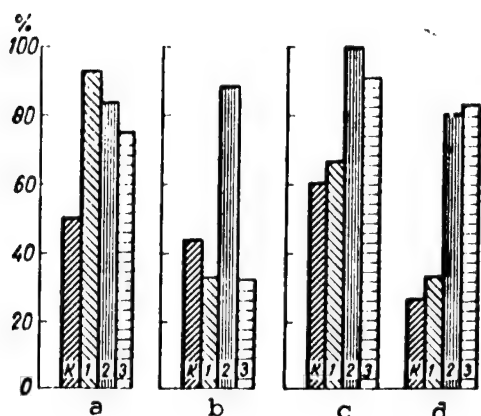
Figure 1.
Effect of dibasol (1), AKS-67 (2) and AKS-87 (3) on rat survival following exposure to gravitational accelerations and ligation of common carotid arteries
K) control
a, b) craniocaudal and caudocranial directions, respectively
c, d) 12 and 48 h after ligation

the reverse acceleration vector, whereas agent AKS-67 had a marked protective effect on the animals, regardless of the vector.

Assuming that the main cause of animal death during gravitational loads were cerebrocirculatory disorders (particularly cerebral ischemia with a craniocaudal vector), we checked rat survival at different stages following bilateral ligation of carotid arteries with administration of the tested agents. In control experiments (without use of the agents), 14 out of 23 animals survived 12 h after ligation of carotid arteries, and only 6 after 48 h. With administration of dibasol, animal survival 12 and 48 h later did not differ appreciably from the control (Figure 1c, d). With administration of AKS-67, all 16 rats survived 12 h after ligation of the vessels, and 13 survived after 48 h, which is 3.1 times more than in the control.

Preadministration of AKS-67 also prolonged the animals' life. Thus, 11 out of 12 rats survived 12 h after ligation of the vessels, and 10 survived after 48 h.

Table 1. Dynamics of changes in PP in vessels of the brain, hind limb and SBP (% of baseline; M±m) in postischemic period in control tests and with use of dibasol

Observation time	Vascular perfusion pressure		Arterial pressure
	brain	hind leg	
Control experiments			
Baseline data, mm Hg	86,7±4,9	92,0±4,8	92,0±7,5
After ischemia:			
after 5 min	— 30,5±4,0*	— 25,8±4,2*	— 20,8±10,6
" 30 "	— 2,3±5,8	— 11,7±17,5	— 35,5±11,7*
" 60 "	+ 28,7±10,6*	+ 13,0±17,3	— 37,2±11,3*
" 120 "	+ 54,2±17,9*	+ 29,5±9,6*	— 40,8±16,8*
Dibasol			
Baseline data, mm Hg	120,5±6,6	118,1±5,9	104,4±5,6
After ischemia:			
after 5 min	51,9±2,5***	— 51,5±4,3***	— 56,1±4,8***
" 30 "	— 32,3±3,5***	— 27,8±9,2*	— 42,0±10,3**
" 60 "	— 10,7±5,2	— 11,3±11,1	— 40,1±10,1**
" 120 "	+ 4,2±8,5	+ 0,3±9,1	— 30,1±12,2*

Here and in Table 2: *P≤0.05, **P≤0.01, ***P≤0.001.

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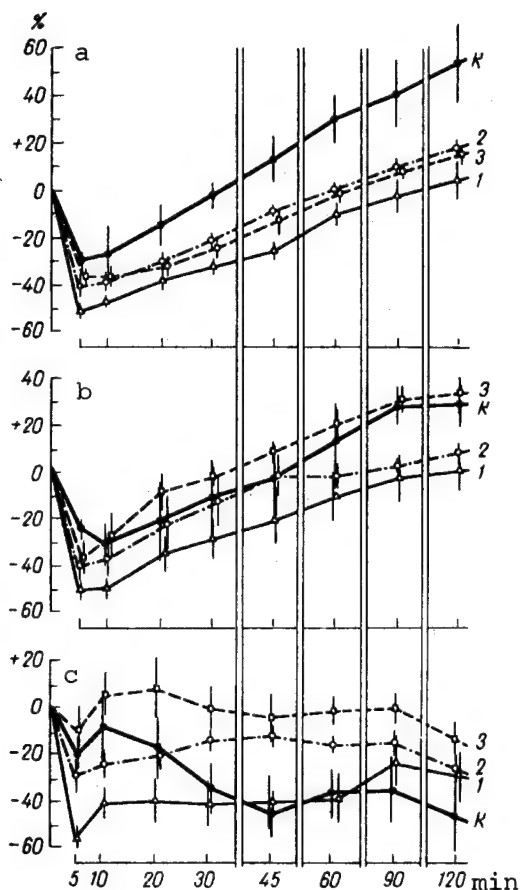
Figure 2.
Dynamics of PP changes in vessels
of the brain (a), posterior extremity
(b) and SBP (c) in anesthetized cats
in the postischemic period
  X-axis, observation time (min)
  K) control
  1, 2, 3) with use of dibasol,
        AKS-67 and AKS-87,
        respectively

A comparison of the results of the experiments with ligation of carotid arteries and gravitational accelerations, which cause cerebral ischemia, revealed a distinct correlation with the protective effects of AKS-67 and AKS-87. However, dibasol had a mild effect in the case of ligation of carotid arteries, whereas it was quite significant in the case of accelerations. Evidently, expression of the protective effect of the tested agents in the case of gravitational overloads concerns the entire cardiovascular system, in particular the mechanisms controlling SBP and tonus of peripheral vessels. In this regard, it is interesting to test the effect of the agents under study on dynamics of changes in SBP, tonus of cerebral and peripheral vessels in the postischemic period. We assessed vascular tonus on the basis of PP changes during isolated autologous blood perfusion of cerebral and peripheral (posterior extremity) vessels using a stable volume of blood (resistographic method).

The results of control experiments on cats [3] revealed that two phases of changes in PP of cerebral vessels are consistently observed in the postischemic period (Figure 2a). The order and duration of these phases conform to the postischemic cerebrovascular phenomena described in the literature. The first phase--decline of PP for 20-30 min--corresponds to the hyperperfusion phenomenon (reactive hyperemia), the second--elevation of PP--started 30-40 min after ischemia and lasted to the end of the experiments (more than 120 min). It corresponds to the hypoperfusion phenomenon, during which there is significant decrease in blood flow. Analogous PP changes were also observed in peripheral vessels, the only difference being that the second phase was less marked (Figure 2b). SBP was unstable for 10-20 min after ischemia and had a tendency toward hypotension, which subsequently progressed and consistently persisted to the end of the experiments (Figure 2c).

Preliminary administration of dibasol and its imidazo analogues intensified the first phase of postischemic PP changes, i.e., it was instrumental in manifestation of the phenomenon of reactive hyperemia and inhibited development of postischemic hypoperfusion of the brain. AKS-67 and dibasol had an

analogous effect on peripheral vessels, whereas the effect of AKS-87 did not differ appreciably from the control. There were particularly vivid differences in the effects of the tested agents on SBP in the postischemia period. Thus, preadministration of dibasol accelerated onset of postischemic hypotension, whereas AKS-67 inhibited its development considerably and AKS-87 virtually prevented it (see Figures, a, b and c, and Tables 1 and 2).

Table 2. Dynamics of changes in PP in vessels of the brain and hind limb, and CBP (% of baseline, M±m) in postischemic period with use of AKS-67 and AKS-87

Time of observation	Vascular perfusion press.		Arterial pressure
	brain	hind leg	
AKS-67			
Baseline data, mm Hg	123,4±4,9	131,7±9,9	96,3±6,9
After ischemia:			
after 5 min	— 42,4±5,3***	— 40,0±7,2***	— 30,1±7,7***
" 30 "	— 21,2±4,1***	— 13,2±11,8	— 15,3±5,1**
" 60 "	+ 2,7±3,5	— 1,1±5,7	— 17,7±34***
" 120 "	+ 19,4±3,5***	+ 9,1±4,7	— 27,5±6,4***
AKS-87			
Baseline data, mm Hg	119,8±6,4	127,5±9,5	82,9±6,1
After ischemia:			
after 5 min	— 36,9±5,9***	— 37,1±7,6***	— 11,0±10,1
" 30 "	— 24,7±5,0***	— 2,9±5,6	— 1,0±10,9
" 60 "	+ 0,9±3,5	+ 20,2±7,4*	— 2,5±6,4
" 120 "	+ 15,7±3,7***	+ 34,5±8,3***	— 14,5±7,3

Thus, along with similar features in their action, there are basic qualitative differences between dibasol and its new imidazo analogues. Further investigation of the mechanism of their action is promising from the standpoint of clinical use of these compounds and search for new analogues. Compound AKS-67, which enhances the body's resistance to gravitational accelerations with both craniocaudal and caudocranial vectors, may be of special interest to aerospace medicine.

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REPRODUCTIVE CAPACITY OF MICROFLORA ON POLYMERS USED IN SEALED ENVIRONMENTS

[Article by N. D. Novikova, M. I. Orlova and M. B. Dyachenko]

[English abstract from source] The main representatives
of human automicroflora were examined to identify the
microorganisms that can grow and develop on various poly-
mers used in an enclosed interior. Bacteria of the genera
Pseudomonas, Proteus and Bacillus were found to be most
proliferative. Microbial growth was strongly influenced
by environmental parameters of the enclosure and by the
chemical structure of the polymer.

[Text] It has been established that microorganisms can accumulate on the
interior surfaces of closed and sealed environments (CSE), their source
being the automicroflora of people in such environments. In recent years,
numerous data have been published [1-4] concerning microorganism capacity to
utilize polymers as sources of food, causing their biodestruction and for
this reason the question of biostability of polymers is rather important in
assuring safe human occupancy of CSE.

The problem of biostability of polymers in long-term CSE can be considered
from the technological and sanitary-hygienic points of view. On the one hand,
it is important to know about the probability of malfunction of different
equipment when microorganisms multiply on its components. On the other hand,
one must consider the possibility of reproduction on polymers of conditionally
pathogenic microorganisms and their migration into the air environment, since
this could have an adverse effect on the sanitary and microbiological situa-
tion in the CSE.

Our objective here was to identify, among the main representatives of human
automicroflora, the microorganisms capable of reproducing on different
groups of polymers used in CSE, as well as to determine the conditions that
are instrumental in this process.

Methods

We tested 10 samples of polymers with different chemical structure that are
used extensively in CSE. We took 10 strains of bacteria isolated from

different surfaces of the interior, equipment and integument of individuals in CSE as test cultures of microorganisms.

A sample of material 5×5 cm in size was placed in a vacuum desiccator 3.5 ℓ in size, on the bottom of which we first decanted 40 mℓ liquid medium containing a specific amount of test microorganisms. We conducted two series of experiments. In the 1st series, a condensate of atmospheric moisture from the CSE was used as liquid medium. This choice was made because it is possible for condensation moisture to get on interior surfaces during operation of a life-support system when people spend time in closed environments [5]. In the 2d series, we used a nutrient-deficient medium without carbon source, which was prepared according to [6]. Absence of carbon in this medium caused microorganisms to utilize polymer material as the missing source of carbon. In control tests there were no samples of polymers. The specimens were allowed to stand from 30 to 60 days at different temperatures. Periodically during incubation we counted test microorganisms by the methods generally used in sanitary bacteriology.

Results and Discussion

Representatives of Gram-negative and Gram-positive bacillary flora (in particular, bacteria of the genera Pseudomonas, Proteus and Bacillus) had a greater reproductive capacity on polymers than representatives of coccal flora. This was probably related to the fact that the former had a rich and diverse set of constitutive and adaptive enzymes causing breakdown of low- and high-molecular compounds and their utilization as sources of nutrition.

quantity/mℓ
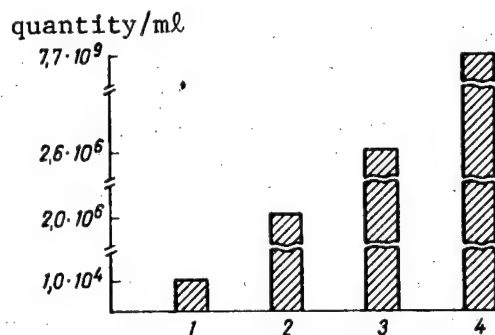
Reproduction of P. aeruginosa on different types of polymers
  1) initial P. aeruginosa content (per cm^2 material)
  2, 3, 4) P. aeruginosa content after 30 days on a system of epoxy enamels, capron cloth and natural suede, respectively

Bacteria of the species Pseudomonas aeruginosa multiplied the most actively on polymers (see Figure); they are often demonstrable on human integument and can be the cause of diverse diseases. They reproduced the most actively on natural suede, i.e., on a material based on protein (see Figure). There was less intensive reproduction on caprone [polycaprolactam plastic] fabric and a system of epoxy enamels, which is indicative of the effect of chemical structure of a polymer on this process. It must be stressed that reproduction of microorganisms on polymers was associated with some changes in their biochemical activity. Thus, after 30-day incubation of P. aeruginosa on real suede, we observed an increase in phosphatase and DNAase activity, as compared to baseline data.

These are preliminary findings; however, the data are sufficient to conduct deeper investigations in this direction, since the change in biochemical activity of microorganisms may be associated with changes in degree of their pathogenicity for man.

The data on reproductive capacity of Gram-positive and Gram-negative bacillary flora on polymers give us a basis for developing specifications for the choice of appropriate antimicrobial preparations and their use in manned CSE. We should stress the difficulty of such work. It is known that expressly representatives of these groups of microorganisms are the most resistant to most disinfectants and drugs used.

The results indicate that temperature, possibility of condensation moisture and chemical composition of condensate are factors that affect the process of microorganism reproduction on polymers. The base concentration of test bacteria on a material was not the deciding factor in this process.

A temperature of 37°C was optimal for reproduction of microorganisms on polymers. At 20°C, bacterial growth was less intensive.

The results of these investigations are indicative of the significance of condensation moisture of appropriate chemical composition to the process of bacterial reproduction on materials. Such parameters of chemical composition of condensation moisture as high concentration of hydrogen ions (pH), high levels of ammonia and acetone can, according to our data, limit considerably the growth of bacteria on polymers. Changes in chemical composition of condensate upon contact with polymers may also occur when microorganisms reproduce. This enables us to single out two possible mechanisms of biodestruction of polymers: utilization by bacteria of the polymer as nutrient substrate; as a result of effects of chemicals contained in the condensate.

It has been shown that the most favorable conditions for microorganism reproduction are provided on heterochain polymers, which include compounds containing in the main chains, in addition to atoms of carbon, atoms of oxygen, nitrogen, sulfur, phosphorus and others, i.e., atoms of elements that are usually contained in naturally occurring organic compounds. Thus, a high reproductive capacity was observed on materials based on cellulose and protein. Microorganisms reproduced less actively on polyamides and polyesters. They virtually failed to reproduce on fluoroplastic and foam plastics.

The data we obtained warrant the conclusion that, when reproducing on polymers, microorganisms may use as nutritional substrate not only the base, but additives contained in the polymer, i.e., plasticizers, fillers, stabilizers, etc. Thus, bacteria of the genus Bacillus reproduced on materials based on polyethylene terephthalate only if compounds of cellulose, which is a naturally occurring organic compound, was contained in the material as a stabilizer.

In conclusion, it should be mentioned that the capacity of some samples of heterochain polymers to stimulate growth of microorganisms may persist as well when people occupy CSE. This is confirmed by data obtained in studies within CSE, which revealed more intensive accumulation of microorganisms expressly on materials, on which there was active growth of test bacteria in laboratory experiments.

Thus, our investigations confirmed the validity of the problem of biostability of polymers for manned CSE.

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METHODS

RESTRAINT SYSTEM FOR WAKING MACACA MULATTA MONKEYS DURING POSTURAL TESTS

[Article by V. P. Melnichenko, M. D. Goldovskaya, V. P. Krotov, A. G. Popov,
I. S. Kondakova and N. V. Gorbatenkova]

[Text] Postural tests are a convenient model for investigation of the
distinctions in physiological functions with changes in body position in
relation to the vector of earth's gravity. In recent times, there has been
increased interest in using this model on monkeys, which are philogenetically
close to man and, unlike other laboratory animals, have a vertically
oriented body [1]. Postural tests are difficult to perform on waking
Macaca mulatta monkeys because of their general motor activity, the level of
which depends largely on how the animals are immobilized on the turntable.
We know of a restraint system involving the use of a special suit [2].
The results of our observations revealed that the system of immobilization
must meet the following requirements: it should not cause any pain to the
animal and must reduce to a minimum the effect of factors that elicit dis-
comfort; it must provide for a standard position of the monkey on the
turntable platform; it must prevent passive displacement of the monkey under
the effect of gravity when the turntable is tilted.

For this reason, we developed a restraint system, the principal elements of
which are an immobilization suit, a device that restricts head movements,
a device that restricts the monkey's body movements in orthostatic position
("saddle").

Postural tests were performed on a turntable, the platform of which, which
was made of thick plywood, had an opening through which excrements could be
disposed of and slits for the straps of the restraining suit and cuffs. The
restraining suit (Figure 1), which is made of heavy cotton, consists of a
bib 1, pants 2 and four restraining cuffs for the upper extremities. The
back of the pants (in the region of the ischial tubercles) is cut out.
Straps are stitched to the vest and pants [3]; they are situated on the
shoulders, sides and bottom of the vest, above the crotch opening in the
pants, in the middle and bottom of each pant leg. The straps are stitched
to the pant legs in such a manner as to have one of them slightly above
the knee joint and the other above the ankle when the suit is on the monkey.
There are velcro fasteners along the inside of the bib bottom and outside

of the pants waist *4*. Restraining cuff *5*, which also has straps, is
a velcro fastener too, the two parts of which are stitched to the ends of
the tape.
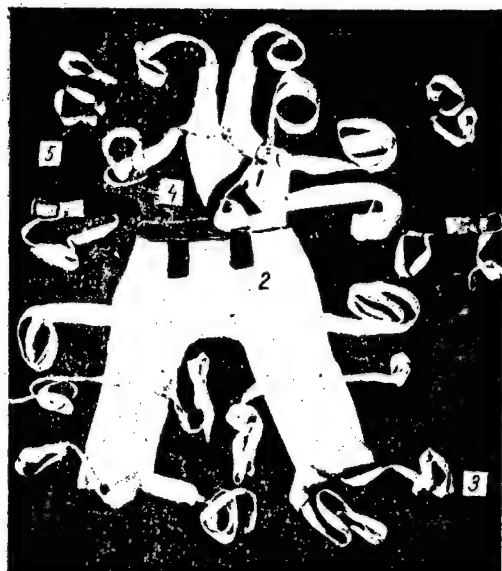
Figure 1.
Suit for immobilizing monkey on
turntable. Explanation given in
the text

Figure 2.
General view of system of immobilizing
monkey on turntable. Explanation given
in the text

The extent of motor restlessness during the test is largely determined by
the way the head is immobilized. In cases where the head remains unrestrained,
the animal constantly tries to get out of the restraint suit. For this reason,
a device was developed that limited the monkey's head movements (Figure 2).
It consists of brace *1* with complex configuration simulating the profile of
the lower jaw and zygomatic tubercles. The brace is secured with a clamp
attached to a bracket that is firmly fixed to the platform of the turntable.
The brace can be displaced in three planes, so that it can be used as a
head restraint for monkeys of different sizes.

When the monkey is turned into antiorthostatic position, shifting of its
body on the table platform under the effect of gravity is restricted by the
shoulder straps. To prevent shifting of the body in orthostatic position, a
special device, a "saddle" (see Figure 2), is used, which consists of
support rollers *3* made of cork or vacuum rubber fitted over metal pins *2*.
The "saddle" is placed in opening *4* for disposal of excrements. Each of
the two pins is attached to bracket *5*, which can be applied against the
metal plate on the bottom surface of the platform by means of a bolt and nut
(not shown in the figure). The brackets with the pins secured in them can
be moved, thus adjusting the position of the rollers and, by tightening the
nut, it can be secured in a specified position.

The procedure for immobilizing the animal is as follows. The monkey is placed supine on the turntable platform, the pants are put on it and then the bib. The bib and pants are joined with the velcro fastener (see Figure 1, 4). The suit straps are passed through the slits in the table platform and tied in pairs. The immobilization cuffs are put on the upper extremities, one slightly above the elbow and the other at the wrist. The velcro fastener of the cuffs is attached, the cuff straps are passed through the appropriate slits in the platform and tied. A pillow-roll is placed under the monkey's head. The brace that restricts head movements is placed in such a manner as to hold the lower jaw and zygomatic tubercles. By moving the brackets of the saddle, the support rollers are placed so that they touch the ischiac callus; then, when the monkey is moved to orthostatic position, it "sits" on them and does not slip off.

The above system was used in postural tests on monkeys weight 3.5-6 kg. The system provided reliable, sparing immobilization of monkeys on the turntable and was convenient to work with.

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METHOD OF DEMONSTRATING CALCIUM IN HUMAN FOOT BY NEUTRON ACTIVATION OF
(α, N)-SOURCES

[Article by V. Ye. Zaychik, A. Ye. Kondrashov and B. V. Morukov]

[Text] Bone demineralization during long-term exposure to weightlessness
and hypokinesia is presently a universally recognized fact. However, it
should be noted that quantitatively incomparable results were obtained with
use of different methods (x-ray densitometry, photon absorptiometry, x-ray
tomography) to determine mineralization of bone. Evidently, this is attri-
butable to the fact that they yield only an indirect estimate of the state
of the mineral matrix of bone, since they characterize a parameter inherent
in bone tissue as a whole, namely, the degree of absorption of photons of x-
ray and γ ranges of energy. Availability of this information alone does not
allow us to draw a strictly quantitative conclusion about one of the important
features of the mineral matrix, the concentration of calcium. Recording
mesoroentgen radiation during exposure of some parts of the skeleton, for
example, the calcaneus, to mu-mesons is a promising procedure for development
of a method of direct measurement of the main mineral constituents of bone [5].
However, there is still much to be done in this direction, and it is difficult
to execute such a measuring method, as well as to make a quantitative inter-
pretation of the obtained results [5, 6].

At the present time, activation by neutrons alone makes it possible to effect
a direct quantitative in vivo assay of Ca in both the entire skeleton and its
different parts. Studies to develop methods of partial in vivo analysis of
Ca with use of neutron sources in ampules began in the late 1960's - early
1970's in Great Britain, Canada and the USSR [8, 9, 11]. By that time, (α, n)-
sources were developed on the basis of ^{238}Pu and sources with ^{252}Cf, which
provided for a yield of up to 10^7-10^8 neutron/s with small dimensions, which
was quite adequate for analysis, according to estimates. In 1974, construc-
tion of a special medical unit was completed at the Scientific Research
Institute of Medical Radiology, USSR Academy of Medical Sciences, for investi-
gations in the field of neutron-activation analysis (NAA) in vivo. The
equipment of this unit, which was intended for partial delivery of neutrons
and highly sensitive spectrometry of radiation from the radionuclides thus
formed, was described in detail previously [1]. Several in vivo NAA methods

were developed on the basis of this unit, in particular, a method of assaying Ca, Na and Cl in stricken parts of long bones of the extremities, which makes it possible to effect differential diagnosis of osteomyelitis and malignant tumors [2].

We submit here a description of the in vivo NAA method for Ca level in the human foot. Special investigations had to be conducted to optimize irradiation conditions and spectrometry, as well as develop special equipment, in order to reach our goal of no more than 0.05 relative total error of each individual measurement with an equivalent dose of no more than 3 rem.

Methods

The method consists in essence of converting the stable nuclide of calcium ^{46}Ca into radionuclide ^{49}Ca, the γ radiation of which is then recorded. Such conversion is obtained as a result of nuclear (n, γ) interactions that arise when the foot is exposed to neutrons. The share of ^{48}Ca in the natural mixture of isotopes is small (0.185%); however, expressly this calcium nuclide has a relatively large section for capture of thermal neutrons (1100 mbarn) and convenient characteristics of the formed radionuclide: $T_{\frac{1}{2}}$ = 8.8 min and E_γ = 3.08 MeV with 89% yield. Under constant conditions of irradiation and spectrometry, the intensity of recorded γ radiation with energy of 3.08 MeV is strictly proportionate to Ca content of the foot. Other radionuclides are also formed in the foot under the effect of neutrons; however, as shown by calculations and previous measurements [6], their radiation does not make a significant contribution to the energy range of 3.08 MeV. The only exception are ^{24}Na γ-quanta with energy of 2.75 MeV, which make some contribution to the analytical photopeak because of inadequate destruction (about 8-12%) in scintillation detectors with large NaI crystals and relatively high intensity. However, this contribution can be taken into consideration if both peaks, 2.75 and 3.08 MeV, are recorded in spectrometry.

A special device (Figure 1) was used to deliver neurons; it consists of a tank (1.5×1.5×1 m) of stainless steel filled with water to the top, surrounded on the sides by lithium-containing screens. The tank is also closed on the top with screens, and they are collapsible in the middle. The cassette with neutron sources is at the bottom of the tank and can be delivered to the desired position in channel-driven carriers ["carts"]. There is a cradle that narrows down toward the foot to support the tested extremity. The wide end of the cradle is attached on hinges to the edge of the chair seat. The support for the foot is adjusted in the cradle to the length of the subject's leg. At the time the subject is seated and the position of his leg fixed using the foot support, the cradle is in horizontal position. During irradiation, the free end of the cradle is dropped to a position that is parallel to the track of the cassette with the sources. There is remote control of the cassette and cradle, by means of rods and cranes. Additional information about the device may be found in [2].

A sketch of the footrest and cassette, as well as their mutual location at the time of irradiation, are illustrated in Figure 2. The cassette is a U-shaped plate of stainless steel on which are secured thin beakers for five ^{238}Pu-Be-sources, type IBN-8-7 (19.5×40 mm) with yield of $5 \cdot 10^7$ neutrons/s

from each. The beakers are equidistant from one another on the perimeter of an ellipse with axes of 300 and 220 mm. The selected dimensions for the ellipse, angle of intersection of the plane of the footrest and cassette, position of the line of intersection of these planes were found by calculation. They are optimal from the standpoint of best uniformity of energy flux of thermal neutrons in the foot at a specified mean level of at least $1.5 \cdot 10^5$ neutron/$cm^2 \cdot$s and on the condition that the minimal distance between any of the sources to the surface of the foot is at least 30 mm. The latter requirement is due to the presence of a drastic increase in ratio of absorbed dose to flux of thermal neutrons near the surface of the sources [2, 3].
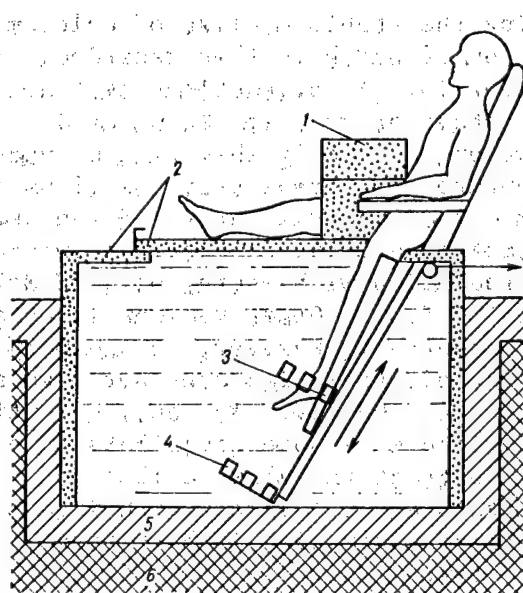
Figure 1.
Device for delivery of neutrons to foot
1) lithium-containing screens
2) stainless steel tank filled with water
3) footrest attached to cradle
4) cassette with neutron sources; arrows show possible movement of cassette
5) concrete pit
6) ground
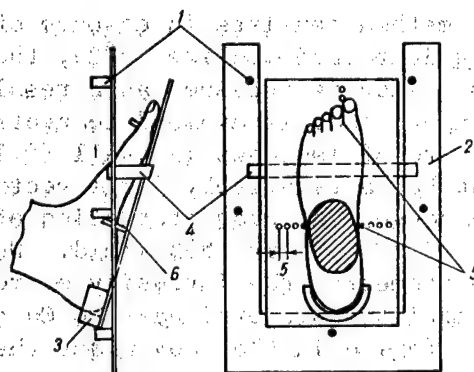
Figure 2.
Mutual location of footrest and cassette with neutron sources at time of irradiation of the foot
1) neutron sources in beakers
2) U-shaped stainless steel plate, on which thin beakers for neutron sources are attached
3) heel rest
4) cassette travel governor
5) removable rods securing foot position
6) rubber ring pressing foot to footrest plane

We used three removable rods, a heel rest and rubber ring attached to the footrest to obtain a steady and reproducible foot position. Reproducibility of mutual location of footrest and cassette during irradiation was provided by means of a governor of cassette travel.

The spectrometry unit consisted of 4 scintillation detectors with 150×100 mm NaI crystal, B5-24 power units, 800-channel LP-840 pulse amplitude analyzer with teletype. Information from each detector was recorded independently by means of an LPE-4867 subgroup selector. The drawing of mutual arrangement of detector crystals is illustrated in Figure 3. A constant and reproducible

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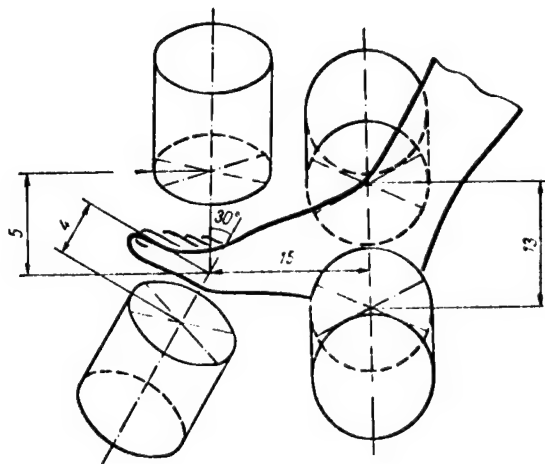
Figure 3.
Drawing of mutual location of
scintillation detector crystals in
spectrometry unit

foot position was provided during the measurements by the footrest and leg cradle attached to the shell of the spectrometry unit. The design of the footrest was similar to the one used for irradiation.

We used previously obtained data [3] to calculate equivalent dosage and distribution of energy flux of thermal neutrons in the foot with the selected mutual location of the foot and sources.

The influence of inaccurate reproduction of geometry of irradiation on results of analysis was assessed by the relative change in mean flux energy of thermal neutrons in the foot calculated for a normal cassette position and for the position when its plane is shifted in parallel by 5 mm. The influence of inacurate reproduction of foot position in spectrometry was evaluated by calculating mean effectiveness of recording γ-quanta arising in the foot. Calculations were made for normal footrest position and for the position where the rest was elevated by 5 mm at the heel. In the calculations, the foot was approximated to a solid wedge, in which we inscribed the human foot up to 30 cm long. All calculations were made on PDP-14 and EC-1033 computers.

Statistical error of individual measurements was evaluated on the basis of data in the literature concerning mean Ca content in the foot of a "standard" man [7] and using the time modes selected for analysis: irradiation 10 min, interval between end of irradiation and start of measurement 2 min, measurement 10 min.

In order to appraise actual error levels, we measured Ca level in 5 essentially healthy men, in their left foot, taking two readings at a 13-day interval, without use of any stimuli. We also measured the volume of the foot (volume circumscribed by the plane of the foot and a parallel plane at a distance of 8 cm), maximum foot length and area. A correlation analysis was made of these parameters and Ca level.

Results and Discussion

As shown by our calculations, when irradiating the largest foot (30 cm in length), maximum energy of absorbed dose from neutrons and γ-quanta constituted 1.62 and 1.14 rad/h, respectively. These dose energies were present only on some superficial parts of the foot, whereas the mean values over the volume of the foot were 0.55 and 0.75 rad/h, respectively. For a smaller foot, maximum and mean absorbed dose energy levels were lower. If we take 10 as the quality factor for neutrons, the overall equivalent dose rate will be 17.3 rem/h as the maximum and would not exceed 6.25 rem/h as the mean. Hence, with the selected duration of exposure, i.e., 10 min, mean equivalent dosage does not exceed 1.05 rem and maximum 2.9 rem.

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Results of in vivo NAA for Ca in the foot

Subject	Measurement No	N_{Ca} counts/10 m	N_Φ c/10 m	N_{Na}^{Ca} c/10 m	$\delta_{ст}$ %	N_{Ca}^1/N_{Ca}^2	δ %	$\delta_{ост}$ %	$\bar{N}_{Ca}^i/N_{Ca}^{Z.V.Ye.}$
Z.V.Ye.	1	1415	473	62	2,90				
	2	1473	461	45	2,79	0,961	4,01	2,82	1,00
S.V.D.	1	1137	460	71	3,51				
	2	1143	469	72	3,41	0,995	0,53	3,42	0,789
K.G.M.	1	1495	457	68	2,87				
	2	1450	471	74	2,93	1,031	3,06	0,98	1,020
K.V.M.	1-	1413	445	73	3,02				
	2	1401	470	62	2,94	1,009	0,85	2,86	0,974
K.V.Ye.	1	1153	483	64	3,56				
	2	1210	465	78	3,47	0,953	4,82	3,29	0,818

Key: N_{Ca}) intensity of analytical part of ^{49}Ca photo peak less background N_Φ and contribution of ^{24}Na photo peak (2.75 MeV) in this region (N_{Na}^{Ca})

δ_{CT}) statistical error of individual measurement of intensity of ^{49}Ca photo peak

N_{Ca}^1/N_{Ca}^2) ratio of intensities of photo peaks of same subject in first and second series of measurements

$\delta = (1-N_{Ca}^1/N_{Ca}^2)$ 100%--total relative error of single measurement characterizing reproducibility of results

$$\delta_{ост} = \sqrt{\left| \delta_{ст}^2 - \delta^2 \right|}$$

$N_{Ca}^i/N_{Ca}^{Z.V.Ye.}$) ratio of Ca level in subject's foot to its level in subject Z.V.Ye.

The energy of thermal neutron flux calculated and confirmed by measurements constituted a mean in the foot of $1.8 \cdot 10^5$ neutron/cm$^2 \cdot$s, while mean effectiveness of recording γ-quanta with energy of 3.08 MeV was 0.055. The background level in the chosen part of the analytical photo peak was 45 counts/m. Using these results, as well as data on weight of foot bones, which constitutes 5.8% of skeleton weight in an adult male weighing 80 kg [7] and the selected times of analysis, we estimated the statistical error of measurement at 3.6%.

The calculated relative error of analysis results due to parallel 5-mm shift of the cassette with neutron sources from its normal position during irradiation constituted 2.6%. A 5 mm elevation of the plane of the footrest on the side of the heel in spectrometry led to relative error of 4.2% in the result. Hence, the overall error of measurement due to such noticeable changes in foot position during irradiation and measurement should not exceed 4.9%, while maximum overall error in the results along with statistical error should not exceed 6%.

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The results obtained with NAA in vivo for Ca in the foot of subjects are listed in the Table.

The coefficients of correlation of calcium level with length of foot, its area and foot volume are 0.75, 0.53 and 0.50, respectively.

Maximum relative error of a single measurement, assessed by reproducibility of result upon repeated analysis did not exceed 4.82%. Maximum statistical error of measurement of intensity of analytical photo peak was about 3.5% and occurred with in vivo NAA in the subject who weighed the least--70 kg-- and whose foot was 25 cm in length. Parameter δ_{OCT} (see Table) attributable mainly to the degree of reproducibility of geometry of irradiation and spectrometry did not exceed 3.4%, which is substantially less than estimated (4.9%).

Since δ_{CT} and δ_{OCT} (see Table) are comparable in value, further refinement of the method should proceed along the lines of reducing both these errors. The statistical error could be reduced by changing time modes of analysis and increasing neutron flux. Thus, only an increase in duration of measurement from 10 to 20 min leads to 15% reduction of δ_{CT}, lowering it to 3%. The 5-fold increase in integral neutron yield with exposure lasting 2 min, which is possible with the biological protection of the unit, and increase in measuring time to 20 min make it possible to lower δ_{CT} to 2.5% with the same radiation burden, and with irradiation for 4 min (2-fold increase in equivalent dose), to 1.7%. The accuracy of reproducing the position of the foot during irradiation and measurement is limited to 2-3 mm due to the non-absolute flexibility of the human body. If attainment of this level of accuracy permits lowering δ_{OCT} to the achieved minimal level for δ_{CT}, the overall error of the in vivo NAA method for Ca in the foot would be 2-2.5%.

The mean equivalent dose in the foot during in vivo NAA for Ca is about 1 rem. This relatively low radiation burden makes it possible to perform the examination three times a year, if necessary [4]. It should be noted, however, that the equivalent dose of 1 rem which we found is substantially exaggerated, since we used the quality factor for fast neutrons, which is 10, to estimate it, and it is valid for chronic irradiation of the entire body. In the case of acute irradiation of a small part of the limb, the quality factor for fast neutrons is considerably lower in the opinion of a number of researchers. This made it possible, for example in [10], to consider it to be 5. With such a variant of calculation the equivalent dose for in vivo NAA of Ca in the foot is only about 0.5 rem, and is virtually comparable to the dose burdens associated with a routine roentgenological examination.

The high value of the obtained information, good accuracy of results, low radiation burdens, availability of needed equipment and relative simplicity of analysis enable us to recommend the developed method, not only for use in space medicine, but in clinical practice, particularly in cases where an objective evaluation of the condition of the skeleton is needed.

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DIRECT SPECTROPHOTOMETRIC METHOD OF ASSAYING AMMONIA CONCENTRATION IN GAS
ENVIRONMENT OF SEEDING CHAMBERS

[Article by A. A. Polovinkin and A. N. Kravchuk]

[Text] Toxicologists have been traditionally using colorimetry methods to
measure ammonia concentration in the air environment: the method of Nessler
[1], a method based on the indophenol reaction [3], alkalimetric [4] and enzyme
[5] methods, etc. Colorimetric methods are simple to use, they have rather
high sensivity and accuracy. However, they also have a number of flaws. In
the first place, these are methods for periodic monitoring. In addition, they
furnish the mean concentration for the period of air sample collection, which
does not permit determination of drastic fluctuations of ammonia concentrations
in the gas atmosphere of chambers. In the second place, frequent collection of
air samples from small chambers results in reduction of ammonia concentration
in the chamber. In the third place, there may be substances in the analyzed
atmosphere that are able, along with ammonia, to interact with color-forming
reagent. For example, hydrogen sulfide and amino compounds distort the
results of analysis obtained by the Nessler method. Use of a spectrophotometric
method of assaying ammonia in an air environment eliminates these flaws.

We have developed and are successfully using a combined unit for measurement
of ammonia concentration in the range of 1-150 mg/m^3 in the atmosphere of
seeding [or priming] chambers in toxicological experiments. The method is
based on using the absorption maximum of ammonia at a wavelength of 204.3 mm
[6]. The unit is equipped with a domestic SF-26 spectrophotometer, which
enables us to work in the ultraviolet part of the spectrum. The spectro-
photometer contains specially developed gas trays, the arrangement of which
is illustrated in Figure 1. The housing of the tray 2 is cylindrical in
shape and made of brass. In order to reduce adsorption of trace impurities
by the tray surface, there is a teflon tube 3 that is pressed into the housing.
Quartz glass holders 4 with glasses 5 are screwed to the ends of the housing.
The tray has a base 6 for installation in the instrument and coupling 1 for
input and output of gases. The absorbing layer of gas in the tray is 110 mm
thick. Figure 2 illustrates a general drawing of the unit. Air from the
tested object 1 is fed into tray 3, which is situated in the tray compartment
of the spectrophotometer 2 by means of teflon line 5. The outlet of the

tray is connected to a diaphragm-type pump *7*, which returns the air into the chamber via return line *6*. A digital voltmeter *9* is connected to the electric outlet of the spectrophotometer to improve precision of readings, as well as automatic recorder *8* for continuous recording of concentrations.
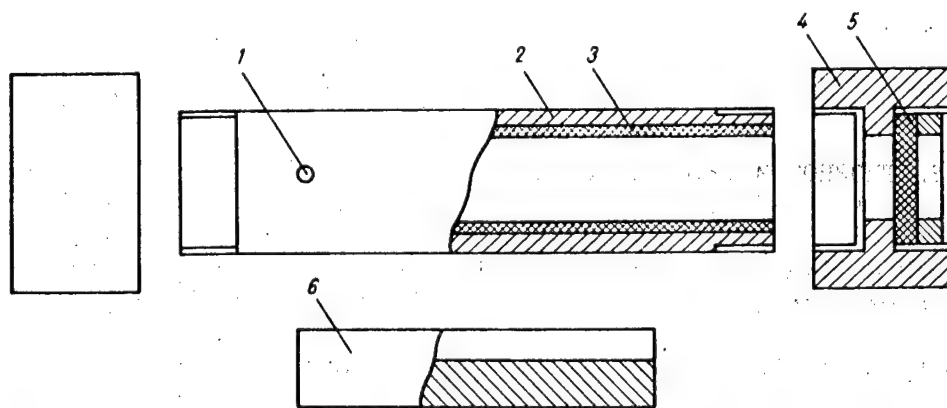

Figure 1. Arrangement of gas tray for SF-26 spectrophotometer

1) coupling
2) tray housing
3) teflon tube

4) glass holder
5) quartz glass
6) base of tray
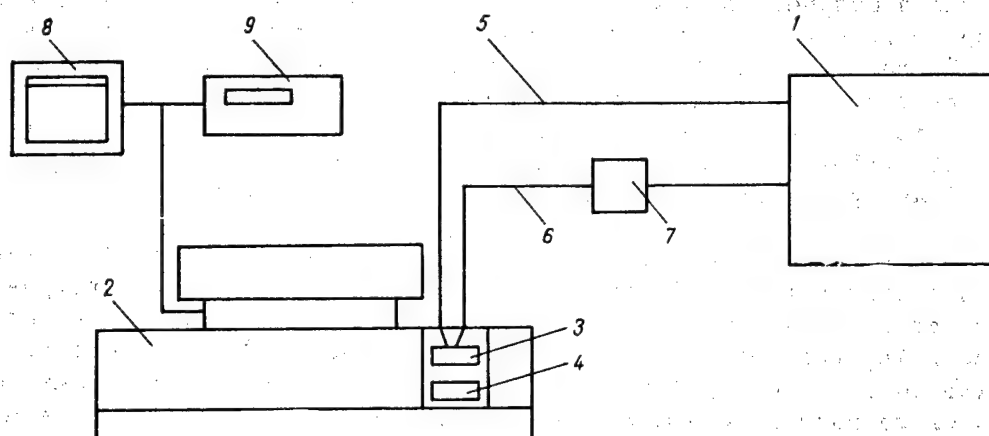
Figure 2. Block diagram of unit for measuring ammonia concentration in gas environment of seeding chambers

1) seeding chamber
2) SF-26 spectrophotometer
3) measuring tray
4) comparison tray
5) input line

6) return line
7) diaphragm pump
8) automatic recorder
9) digital voltmeter
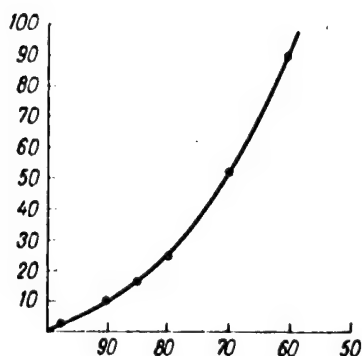
Figure 3.
Coefficient of transmission as a
function of ammonia concentration
in the chamber
   X-axis, transmission coeffi-
   cient (%); y-axis, ammonia
   concentration (mg/m^3)

The instrument was calibrated for mixtures
of ammonia with dry nitrogen. For control
readings of ammonia concentrations we
used the Nessler method. With ammonia
concentrations in the atmosphere of the
chamber of 2, 5, 10, 16, 24, 52 and 88 mg/
m^3, the transmission coefficient was 98,
90, 85, 80, 70 and 60%, respectively. The
margin of error in measuring the trans-
mission coefficient did not exceed 0.5%.
Figure 3 illustrates the curve of the
transmission coefficient as a function of
ammonia concentration.

We used standard ammonia-nitrogen mixtures
in concentrations of 7 and 38 mg/m^3, which
were obtained on the Microgas instrument,
to estimate error of measuring concentra-
tion. The margin of error in measuring
ammonia concentration in these mixtures did
not exceed 5%.

It is important to mention that when the ammonia concentration exceeded sig-
nificantly that of impurities that are constant constituents of the atmosphere
of manned closed environments [2], the presence of the latter had virtually
no influence on accuracy of measurement.

Introduction of the above-described device to practical toxicological studies
makes it possible to effect continuous monitoring, recording and correction
of ammonia content of seeding chambers.

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AMINO ACID SPECTRUM OF HUMAN BLOOD IN THE PRESENCE OF EMOTIONAL STRESS

[Article by T. F. Vlasova, A. S. Ushakov, V. P. Bychkov and
Ye. B. Miroshnikova]

[Text] We submit here the results of assaying the amino acid spectrum of
human blood with simulation of stress situations similar to the professional
activities of cosmonauts.

Methods

A total of 5 healthy men 23 to 41 years of age participated in the studies.
Neuro-emotional stress was produced by means of three models of stress situa-
tions. In the first model, simulated ascent to 8000 m in a pressure chamber
was used as the stressor, in the second, anticipation of gravitational
accelerations on a centrifuge (C) and in the third, performance of assigned
mental work with a time limit under conditions of "success" and "failure"
situations. On the day prior to the studies, at 1200 hours, the subjects
were informed of what they were to do. Ascent was simulated by means of
appropriate sounds in a GBK-63 pressure chamber, in which we installed an
altimeter connected to a vacuum pump, so that the subjects were able to
observe their "altitude." Prior to the second stress situation, the subjects
were informed that they could be rotated on a centrifuge with accelerations
of up to 8 G, then this rotation was cancelled at 1100 hours the following day.
In the third stress situation, the subjects were asked to pick an assignment
among several differing in difficulty, each of which involved working with
coded symbols for time and solution of logic problems (G. Ayzenko number
test). This test was made with the researcher giving verbal instructions and
it enabled us to assess the subjects' intellectual qualities, along with their
reaction.

Before and after the stress situations, we assayed 14 free amino acids in
fasting blood plasma drawn from the ulnar vein. The amino acids were
recorded on a Hitachi KLA-3B automatic analyzer (Japan, sensitivity of
instrument 0.1 μmol) using ion-exchange chromatography [2, 8]. The tested
samples were first deproteinized with crystalline sulfosalicylic acid [7].

Free amino acid levels in blood plasma of subjects under stress (mg%)

Amino acid	Baseline period	Simulated pressure chamber		Simulated centrifuge		Psychological test	
		before	after	before	after	before	after
Isoleucine	0.73±0.03	0.17±0.01*	0.21±0.03*	0.63±0.06	0.73±0.04	1.37±0.09	0.94±0.07
Leucine	1.37±0.08	0.34±0.02*	0.46±0.06*	1.16±0.11	1.30±0.05	2.06±0.15*	1.74±0.08*
Valine	1.93±0.09	0.40±0.14*	0.56±0.05*	1.65±0.23*	1.65±0.12*	2.88±0.20*	2.31±0.19
Threonine	1.38±0.12*	0.30±0.03*	0.36±0.03*	1.75±0.17	1.45±0.24	1.28±0.10	1.83±0.22
Serine	1.31±0.07	0.29±0.02*	0.33±0.10*	1.22±0.17	1.34±0.10	1.22±0.23	1.50±0.14
Methionine	0.24±0.05	0.08±0.01*	0.10±0.02*	0.19±0.04	0.24±0.04*	0.42±0.04*	0.39±0.02*
Tyrosine	0.79±0.07	0.17±0.02*	0.28±0.06*	0.59±0.06*	0.64±0.03*	1.08±0.09*	0.99±0.05
Phenylalanine	0.70±0.05	0.17±0.02*	0.31±0.07*	0.50±0.02*	0.60±0.04*	1.05±0.03*	0.85±0.07
Cystine	0.70±0.04	0.25±0.03*	0.15±0.02*	0.43±0.05*	0.44±0.05	0.39±0.04*	0.44±0.05*
Aspartic acid	0.12±0.03	0.04±0.01*	0.06±0.01*	0.14±0.03	0.15±0.03	0.91±0.07*	0.59±0.04*
Glutamic acid	2.15±0.08	1.18±0.09*	1.45±0.10*	1.66±0.17	1.58±0.16*	3.06±0.08*	8.87±0.16*
Proline	2.11±0.08	1.21±0.07*	1.13±0.07*	1.61±0.10*	1.46±0.22*	2.33±0.08	2.41±0.13
Glycine	1.36±0.11	0.39±0.04*	0.50±0.07*	1.11±0.15	1.37±0.11	2.23±0.17*	2.10±0.13*
Alanine	2.27±0.12	0.51±0.05*	0.65±0.09*	1.93±0.05*	1.65±0.10*	3.17±0.29*	3.10±0.17*
totals	17.2	5.5	6.6	14.6	14.6	23.5	28.1

*Results are statistically reliable as compared to baseline.

Results and Discussion

Data on levels of free amino acids in subjects' blood plasma, demonstrated
with different models of stress situations, are summarized in the Table. A
comparison of the results before and after each model was made in relation
to baseline data, which were within the range of the physiological norm. We
see from the results listed in this table that simulation of ascent elicited
a substantial reduction in the free amino acid pool as a result of decline of
levels of all tested amino acids, both before and after the model. Total
amino acid content before and after use of models constituted 5.5 and 6.6 mg%,
respectively, versus 17.2 mg% in the baseline period. Anticipation of gravi-
tational accelerations on the centrifuge led to a decrease in free amino acid
pool in blood, but to a lesser extent than with the first model. There was
reliable drop in levels of valine, phenylalanine, tyrosine, cystine, proline
and alanine, the concentrations of which remained low after the stress situa-
tion. The demonstrated reduction of the amino acid pool in blood under
the effect of the two stress models was analogous to the previously found
changes in amino acid composition of human blood plasma during stays in a
confined pressure chamber [1] and in individuals whose occupation involves
emotional stress. Increased utilization of free amino acids under stress
is the body's natural reaction, and it is consistent with the conventional
conceptions of the physiological role of amino acids as the body's reserve,
involvement of which increases dramatically in numerous reactions of inter-
mediary metabolism at the time of exposure to the situation. In that study,
there was an increase in blood albumin concentration [3], and for this reason
it can be assumed that the decline of blood amino acid levels is related to
their participation in synthesis of albumins as the most labile proteins.
In addition, simulation of ascent and anticipation of gravitational accelera-
tions on the centrifuge as stress factors elicited slowing of gluconeogenesis
in the liver, as conformed by the decrease in plasma alanine concentration,
which is the precursor of gluconeogenesis [5, 6]. The subjects' reaction to

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the psychological test was not stressful and, on the contrary, led to increase in amino acid pool of blood due to increase in concentration levels of most amino acids, particularly glutamic acid, the level of which was 3 times higher than in the baseline period. This response is related to the fact that, during mental tension, there is intensive metabolism of glutamic acid in the brain [4].

Thus, our investigations enabled us to demonstrate consistent changes in amino acid spectrum of human blood, which depended on the nature of the stress situation. It was shown that the mere simulation of an ascent and anticipation of gravitational accelerations on a centrifuge are stressful and elicit similar changes in amino acid spectrum of blood. The psychological test led to a shift of blood amino acid equilibrium that is inherent in individuals whose occupation involves mental tension.

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BLOOD SERUM ENZYMES DURING 7-DAY WATER IMMERSION

[Article by T. Ye. Drozdova and Ye. G. Vetrova]

[Text] During submersion in water the body is exposed to a number of factors,
among which redistribution of blood and lack of load on the locomotor system
are rather important. This could affect metabolism of skeletomuscular
tissue and parenchymatous organs, analogous to the effect of weightlessness.
Investigation of changes in blood serum enzyme spectrum enables us to
demonstrate, with some degree of certainty, the direction of metabolic
transformations in different tissues and organs in weightlessness.

Methods

The studies were conducted on 6 healthy men 25-35 years of age who spent 7
days immersed in water using the dry submersion method [4]. Baseline studies
were performed twice: 5 days (baseline 1) and 2 days before the start of the
experiment. The tests were then repeated on the 2d, 4th, 7th days of immer-
sion and 2d and 5th days of the recovery period. Using the test sets of
the Boeringer firm, we measured activity of the following enzymes in blood
serum: NAD-dependent malate dehydrogenase (MDH), NADP-dependent isocitrate
dehydrogenase (ICDH), alanine aminotransferase (ALT), aspartate aminotransfer-
ase (AST), creatine phosphokinase (CPK) and its isozymes, as well as distribu-
tion of isoforms of MDH [3].

Results and Discussion

We determined the baseline level of ALT, AST, CPK, MDH, ICDH and isozymes of
MDH and CPK 5 and 2 days before the experiment (see Table). On the 2d day
of water immersion there was insignificant decrease in MDH and ALT activity.
CPK activity increased reliable at the expense of MM isoforms (in relation
to baselin 1 level); AST, ICDH activity and ratio between MDH isozymes did
not differ from baseline values. By the 4th day of water immersion, we ob-
served further decline of MDH and ICDH activity, which was statistically re-
liable in relation to baseline 1. CPK, ALT, AST activity and distribution of
MDH isozymes did not differ from baseline values. On the 7th day of the
study, the decline of activity constituted 14% for MDH, 20% for ICDH and 25%
for MM CPK (as compared to baseline 1 activity). The decrease in ALT activity

and total CPK activity was not statistically reliable. AST activity and distribution of MDH fractions did not undergo appreciable change. By the 2d day of the recovery period there was increase in activity of serum enzymes, by 88% for ALT, 50% for CPK, 68% for isoforms of MM CPK, 13% for MDH and 17% for ICDH, as compared to the data obtained in the last analysis during water immersion. On the 5th day of the recovery period, there was further increase in activity of CPK, MDH and ICDH. ICDH and MDH activity reached the baseline 1 level, while CPK activity exceeded it by 36%.

Activity of ALT, AST, ICDH, MDH, CPK and isozymes of MDH and CPK in blood serum (M±m)

Parameter	Day before immersion		Day of immersion			Day after immersion	
	5	2	2	4	7	2	5
ALT	16,0±3,3	15,6±4,7	13,4±1,6	16,0±2,4	13,9±1,6	26,1±2,9*,**	17,9±2,7**
AST	11,3±1,0	12,1±0,8	11,4±0,8	12,3±0,8	11,7±1,3	13,8±1,2*	10,2±0,7
Total CPK	19,1±2,4	22,4±2,6	21,7±2,7*	19,8±2,4	16,5±2,6	24,8±3,9**	26,0±1,7**
CPK MM	17,0±1,1	19,8±2,2	20,7±1,2*	18,0±1,3	12,7±0,6	21,3±1,1**	21,2±1,0**
CPK MB	2,1±0,4	2,6±1,6	1,0±0,4	1,8±0,5	3,8±0,8	3,5±0,6	4,8±0,9
ICDH	4,2±0,5	3,6±0,3	3,5±1,3	3,1±0,9*	2,9±0,7*	3,4±0,2	4,1±0,4**
MDH	80±4,9	79±1,5	75±3,5	72±4,7*	69±4,4*	78±5,7	87±8,1**
MDH1	16±1,0	17±1,5	17±1,3	17±1,7	18±1,6	16±1,6	17±1,4
MDH2	19±3,4	21±2,6	21±2,5	21±2,8	22±2,9	22±3,0	22±2,5
MDH3	65±3,3	62±3,8	62±2,6	62±3,1	60±3,6	62±3,5	61±2,9

*Probability of difference between data obtained during immersion and in recovery period, as compared to baseline 1; P<0.05.
**Probability of difference between data obtained in recovery period and 7th day of immersion; P<0.05.

Thus, 7-day water immersion was associated with decline in activity of MDH, ICDH and CPK at the expense of isoforms of MM in the absence of changes in AST activity and distribution of MDH isoforms. The decline in activity of oxidative enzymes MDH, ICDH in blood and enzyme of energy metabolism of muscle tissue, CPK, is probably a reflection of the diminished activity of enzymes in skeletomuscular tissue due to decrease in its functional load and in intensity of metabolism as a whole during immersion. The noted changes may be indicative of diminished intensity of energy metabolism in tissues due to inhibition of intracellular activity of enzymes of the Krebs cycle and CPK by the surplus of ATP, which could accumulate when there is insufficient muscular exertion. The decrease in CPK activity during immersion due to the MM fraction, which was highly reliable, is indicative of skeletomuscular localization of the indicated changes [2].

A return to active motor function requires tension of systems upon which vital functions depend, in particular, intensification of processes of energy production in skeletomuscular tissue which, in turn, is provided by activation of several enzymatic reactions in tissue. This determines the adaptive nature of the observed biochemical changes.

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INTENSITY OF PHOTOSYNTHESIS IN CLOSTERIOPSIS ACICULARIS VAR. AFRICANA HIND
AS A FUNCTION OF OXYGEN CONCENTRATION IN THE ATMOSPHERE

[Article by M. A. Levinskikh]

[Text] When unicellular algae are included in the photoautotrophic link of
closed ecological systems, it is important to know their attitude toward
different concentrations of oxygen in the atmosphere. The adverse influence
of high concentrations of oxygen on photosynthesis is known as the Warburg
effect. The inhibitory effect of high oxygen content on photosynthetic
productivity of algae referable to different taxonomic groups has been
repeatedly confirmed by many authors [1, 5, 8]. In particular, for a
number of Chlorella strains it was shown that intensity of photosynthesis,
in the case of both cumulative and continuous long-term cultivation, is
directly related to concentration of oxygen in the gas phase [2, 11].

At the same time, there is information to the effect that some algae can
retain productivity when partial oxygen pressure is raised both in the
range of 3-5 to 21% [3, 5] and up to 40-80% [4, 13]. Finally, it was es-
tablished that the photosynthetic process in Chlorella sorokiniana ORS
is resistant to oxygen concentrations in the atmosphere of up to 95% [12, 9].

Our objective was to investigate the intensity of photosynthesis in Clos-
teriopsis acicularis var. africana Hind., family Ankistrodesmaceae, as a
function of oxygen concentration in the reactor's gas phase.

Method

Experiments were performed with intensive cumulative and continuous modes of
cultivation of algae in a rotation-type reactor with about 60 klux illumina-
tion on the surface. Carbon dioxide concentration in the atmosphere was
2-5% with a closed air circuit in the reactor. Other cultivating conditions
for the algae were optimal. We tested oxygen concentrations in the atmos-
phere in the range of 4.5-50.0%. A high oxygen concentration was produced
either by natural, gradual increase in the closed system due to photosynthesis
of algae, or by addition of separate portions into the atmosphere of the
reactor from external sources. This enabled us to prevent algal adaptation
to gradual increase in oxygen concentration during cultivation, as reported
in the literature [13, 6]. We measured the rate of algal growth with different

concentrations of oxygen according to uptake of carbon dioxide from the atmosphere by algae and increase in dry algal substance. Growth rate and photosynthesis of a culture obtained in our reactor with 20-21% oxygen in the atmosphere was taken as the nominal rate (100%). The culture was exposed to high concentrations of oxygen in the atmosphere for 56-65 h in the course of 3.0-3.5 generations.
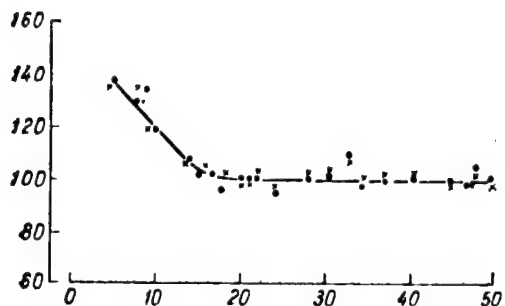
Intensity of photosynthesis in Closteriopsis acicularis according to carbon dioxide uptake (dots) and biomass increment (crosses) as a function of concentration of oxygen in atmosphere
  X-axis, oxygen concentration (%), y-axis, intensity of photosynthesis (%)

Results and Discussion

Analysis of our results revealed that the rate of photosynthesis and growth of algae depends on the oxygen concentration in the atmosphere (see Figure). Maximum growth rate was noted with the minimal oxygen concentration (4.5%) used in our experiments. It was 38% above the nominal rate. With increase in oxygen concentration, the rate of photosynthesis and growth diminished and reached a nominal level with 19-19.5% oxygen in the air. With further increase in concentration of oxygen, growth rate remained at this level up to a 50% concentration of oxygen (the maximum in our experiments). This function remained unchanged with both gradual increase in oxygen concentration due to its accumulation as a result of photosynthesis and addition in portions from exogenous sources. We failed to demonstrate a difference in algal culture reaction to change in concentration of oxygen in the atmosphere when using different cultivation modes (cumulative or continuous).

Thus, it was established that Closteriopsis acicularis algae cultivated under intense conditions are characterized by the Warburg effect, which is manifested by decrease in photosynthesis and growth of algae when oxygen concentration in the atmosphere is raised from 4.5 to 20%. Further increase in oxygen concentration to 50% did not elicit changes in intensity of photosynthesis or productivity of the culture. These findings differ from those previously reported for Chlorella under identical cultivation conditions, where it was found that, in the range of 5 to 50% oxygen concentrations, a 10% increase in atmospheric oxygen led to 15% decline of photosynthesis [2].

Proceeding from the obtained function, it can be concluded that the process of photosynthesis in Closteriopsis acicularis algae is stable when oxygen concentration is raised to above the usual atmospheric level. Consequently, the strain we tested, as is the case for several other algae [3, 4], is closer to higher plants with carbon metabolism in the C_4-dicarboxylic acid cycle, which are also characterized by greater resistance to this factor [10, 7], according to the reaction of the photosynthetic system to high partial oxygen pressure.

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RADIOPROTECTIVE AND THERAPEUTIC EFFICACY OF CARRAGEENAN AGAINST PROTON
RADIATION

[Article by K. S. Chertkov, N. I. Gvozdeva, B. S. Fedorenko and
Yu. Yu. Preobrazhenskiy]

[Text] Assurance of radiation safety of long-term spaceflights is one of the
important tasks put to space biology and medicine. In this regard, importance
is attributed to refinement of technical equipment, search and development of
effective drugs [3, 4].

It is known that the danger of irradiation, mainly from high-energy protons,
is higher in long-term spaceflights. We have encountered very few works
dealing with investigation of radioprotective efficacy in relation to proton
radiation [1, 2].

For this reason, it was deemed desirable to investigate the radioprotective
properties of some previously tested radioprotective agents, for example,
carrageenan [5, 6], during exposure to protons.

Methods

Experiments were performed on 290 male and female hybrid (CBA×C$_{57}$BL) mice
weighing 20-23 g. The animals were exposed to protons with energy of 645 MeV
and intensity of 136.7×10^{-4}-51.6×10^{-4} A/kg or 20-53 rad/s. The radiation
doses were 5, 6, 7 and 8 Gy for control animals, 6, 7, 8, 8.5 and 9 Gy for
experimental ones.

Carrageenan, which is a polysaccharide of plant origin, was recovered from
red Tichocarpus crinitus seaweed with molecular weight of over 100,000. The
latter was given intravenously at the rate of 6 mg/kg 10-15 min before irradi-
ation for protective purposes or in a dosage of 2 mg/kg 6-7 h after irradia-
tion for therapeutic purposes.

Efficacy of carrageenan was assessed according to 30-day survival, dynamics
of body weight, cellularity of bone marrow and number of endogenous colonies
in the spleen on the 9th day after exposure to proton radiation. We conducted
three series of experiments. The findings are summed up in the Table.

Effect on carrageenan on survival of mice exposed to high-energy (645 MeV) protons

Radiation dose, Gy	Intensity, A/kg	Agent dose, mg/kg	Time of injection	Number of mice in group	Survival	
					absol.	%
6	$51,6 \cdot 10^{-4}$	6	10-15 min before irradiation	15	14	93
	$51,6 \cdot 10^{-4}$	2	6-7 h after irradiation	18	12	67
	$51,6 \cdot 10^{-4}$	control	—	19	14	74
7	$51,6 \cdot 10^{-4}$	6	10-15 min before irradiation	27	19	70*
	$51,6 \cdot 10^{-4}$	2	6-7 h after irradiation	21	11	52
	$51,6 \cdot 10^{-4}$	control	—	36	13	36
8	$51,6 \cdot 10^{-4}$ $136,7 \cdot 10^{-4}$	6	10-15 min after irradiation	57	33	58**
	$51,6 \cdot 10^{-4}$ $136,7 \cdot 10^{-4}$	control	—	64	2	3
8,5	$136,7 \cdot 10^{-4}$	6	10-15 min before irradiation	29	2	10

* $P < 0,02$.
** $P < 0,001$.

Results and Discussion

Preventive injection of carrageenan in a dosage of 6 mg/kg 10-16 min before irradiation in doses of 6 Gy ($LD_{26/30}$), 7 Gy ($LD_{64/30}$) and 8 Gy ($LD_{97/30}$) resulted in survival of 93, 70 and 58% of the mice, respectively. In other words, at a dosage close to the minimum lethal dose, the figure was 55% above the control (P<0.001). With doses of 8.5 and 9 Gy, we failed to observe a rise in animal survival rate.

When we determined the therapeutic efficacy of carrageenan, which we tested at radiation doses of 6 and 7 Gy, we demonstrated enhancement of the toxic effect of the product if it was given immediately (within 5-10 min) after irradiation. For this reason, we reduced the carrageenan dosage to 2 mg/kg and postponed administration time to 6-7 h after irradiation. After exposure to radiation in a dosage of 6 Gy, there was no increase in survival of animals treated with carrageenan. A tendency toward manifestation of a therapeutic effect, as manifested by 16% rise in mouse survival, was demonstrated only with use of radiation in a dosage of 7 Gy.

The protective action of the product affected the hemopoietic centers. Thus, the number of nuclear medullary cells in the canal of the femur on the 3d day after irradiation in doses of 6, 7 and 8 Gy constituted 7.1, 6.2 and 3.8 million in the protected groups, respectively, versus 2.6, 2.7 and 2.4 million

cells in control animals. The differences in number of bone marrow cells were particularly distinct with a dosage of 6 Gy (see Figure).
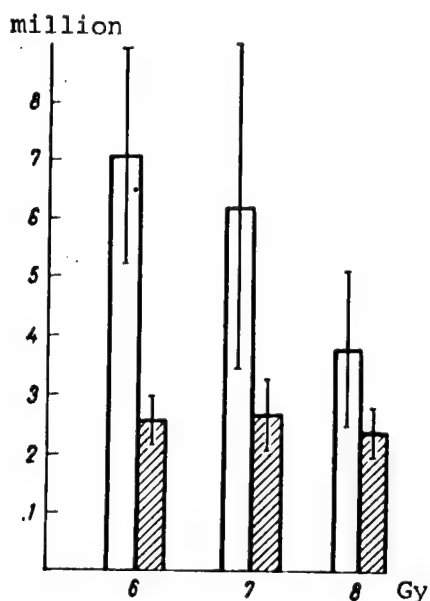
million

Changes in cellularity of bone marrow (millions) in mouse femur with different doses of radiation (in Gy) on the 3d day after exposure to protons
White bars--experimental groups; striped--control. Vertical lines indicate limits of confidence intervals

We used the endogenous cloning method to determine the number of colony-forming cells in the spleen. Only a few colonies appeared in the spleen in the control group after delivery of radiation in a dosage of 8 Gy. The mean number for the group was 0.12 colony. Under the same irradiation conditions, the mean number of colonies was 9.2 in mice protected with carrageenan.

In addition, animals protected with this agent lost less weight, which was manifested particularly on the 7th post-irradiation day, when mean weight of protected mice was 26.2 g versus 22.8 g in the control. By the 14th day, 1 mouse weighing 26 g survived in the control group after exposure to 8 Gy. Mean weight of protected mice was 28.8 g at this time.

Thus, the results of these studies enabled us to establish that carrageenan has radioprotective action against protons, and it was distinctly manifested with delivery of 6 to 8 Gy according to the survival test. Survival rate was 19 to 55% higher in protected mice, as compared to the control.

Under our irradiation conditions, the therapeutic effect of carrageenan on mice was inconsistent.

The obtained figures are indicative of beneficial effect of carrageenan with exposure to protons. One of the possible routes of carrageenan action may be protection of the hemopoietic system, i.e., less damage to stem cells and acceleration of processes of restoration of hemopoietic elements. This is indicated by the larger number of nuclear cells in the femur at the time of maximum cytopenia, as well as the larger number of endogenous colonies in the spleen.

These results are consistent with previously obtained data characterizing the protective properties of carrageenan in the case of γ-radiation [5, 6].

Thus, in experiments on mice the radioprotective properties of carrageenan were manifested with two tested types of radiation. Our findings supplement known information about the high biological activity of carrageenan [7, 8].

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ANNIVERSARIES

SIXTIETH ANNIVERSARY OF FOUNDATION OF PSYCHOPHYSIOLOGICAL LABORATORIES AND NINETIETH ANNIVERSARY OF THE BIRTHDAY OF N. M. DOBROTVORSKIY

[Article by N. Ye. Makhson]

[Text] Nikolay Mitrofanovich Dobrotvorskiy can be included in the pleiad of Soviet scientists who, having accepted unconditionally the October Socialist Revolution, supported with their labor the honor and glory of Soviet science. There is every justification to consider him one of the founders of aviation medicine in our country.

Nikolay Mitrofanovich was born to the family of a professor at the Military Medical Academy (VMA), a colleague of the outstanding Russian neurologist, psychiatrist and psychologist, V. M. Bekhterev. From his childhood years, he absorbed an atmosphere of high culture, scientific debates and opposition to the tsarist regime.

After graduating from VMA in 1916, N. M. Dobrotvorskiy served in a regiment, then in 1918 he returned to the Academy where he worked as an instructor. Even in his student years, he displayed much interest in physiological and clinical research. In 1917-1918, 3 of his works were published, one of which was awarded the VMA gold medal. They were all subsequently published in the German and American press. He devoted particular attention in them to traumatic psychoneurosis, investigation of the effect of mental trauma on the nervous system and psyche of servicemen. The subsequent works of N. M. Dobrotvorskiy dealt with problems of psychiatry, in particular, investigation of the effect of social events on the psychophysical condition of mental patients, as well as healthy individuals. I. P. Pavlov played a large part in shaping the young scientist, and this was reflected by the direction in which N. M. Dobrotvorskiy developed Soviet aviation medicine in the period of its conception. This is also indicated by his published early scientific works ("Biological Diagnostic Methods in Psychiatry"; "Use of Serology in Psychiatry"; "Application of Conditioned Reflex Method to Man," and others).

Already in the first half of the 1920's, Nikolay Mitrofanovich devoted much attention to development of Soviet aviation, psychology of people working in aviation medicine. In his memoirs, he writes: "In the fall of 1921, the

first tests were made of simple reaction time of pilots in the Petrograd Military District at the laboratory in the department of psychiatry. These tests demonstrated to me personally that it is more than rash to draw conclusions about flight service on the basis of simple reaction time.... In a consultation with Academician I. P. Pavlov, I paid attention more to inhibition of reactions by all sorts of transient stimuli than to reaction time...." Students, who were members of a neuropsychiatric scientific club organized under the laboratory that N. M. Dobrotvorskiy headed, participated in these studies.

In 1924, four psychophysiological laboratories of the Air Force were founded, and N. M. Dobrotvorskiy was appointed chief of the Central Laboratory. These laboratories were concerned with the following: investigation of physical and psychophysical condition of flight personnel; screening of applicants to the Air Force using physical and psychophysical data; investigation of working conditions of workers in the aviation service, detection of harmful factors and their elimination. These laboratories were small (the central one was manned by 5 physicians, 1 engineer, 1 instructor-pilot and ancillary personnel), but they performed an enormous amount of work, preparing the foundation for establishment of an institute of aviation medicine. Nikolay Mitrofanovich was extremely serious and conscientious in his approach to establishment of the Central Laboratory. It was necessary to find the appropriate personnel to do this. The selection of individuals among the young physicians who graduated in 1922–1923 turned out to be very good. S. Ye. Mints was appointed deputy chief of the laboratory; he died in performing his service duties, and the laboratory was named for him. The staff of the laboratory--internist P. I. Yegorov, otorhinolaryngologist G. G. Kulikovskiy, ophthalmologist N. A. Vishnevskiy, physiologist A. V. Lebedinskiy and others--subsequently became famous professors and prominent specialists.

Nikolay Mitrofanovich was the first physician-pilot in our country. It is not by chance that he mastered the occupation of pilot. He believed that it was necessary to "make a comprehensive study of both flying and people involved in it" in order to solve the pressing problems of aviation medicine. Nikolay Mitrofanovich learned to fly in order to study working conditions of flight personnel, i.e., "flying itself," and in this sense he developed the traditions of Russian scientists, such as D. I. Mendeleyev. With reference to a flight in a balloon by Academician Ya. D. Zakharov, D. I. Mendeleyev wrote in 1804: "Gay-Lussac made an ascent two months later, and we should be proud of the fact that the first, purely meteorological ascent was made by a Russian scientist from Petersburg," and later he also rode in a balloon.

Nikolay Mitrofanovich was a passionate proponent of objective methods of testing the effects of flight work on the psychophysical state of man. And, although such methods have been insignificantly improved to date and cannot compare with those used by the first Russian researchers in the field of aviation medicine (just as we cannot compare the level of development of aviation in those years to its present level), the basic approach used by N. M. Dobrotvorskiy has retained its relevance.

In 1930-1936, Nikolay Mitrofanovich again served in the ranks of the RKKA [Workers' and Peasants' Red Army] and delivered a lecture course at the Air Force Academy (VVA) imeni N. Ye. Zhukovskiy, which was subsequently published in the form of a monograph under the title of "Flight Work." This was the first book in our country on aviation medicine. In this period, Nikolay Mitrofanovich collaborated closely at the VVA imeni N. Ye. Zhukovskiy with a group that investigated jet propulsion (GIRD), which was headed at that time by S. P. Korolev. In her memoirs, K. M. Vintsentini writes that, in 1932-1933 S. P. Korolev attributed much importance to investigation of the effects of atmospheric pressure and its changes on an individual who will have to fly in the stratosphere and space. By personal agreement of S. P. Korolev and N. M. Dobrotvorskiy, K. M. Vintsentini and N. M. Dobrotvorskiy performed numerous ascents in the pressure chamber of the VVA imeni N. Ye. Zhukovskiy (which they did mainly at the end of the work day, after K. M. Vintsentini, a surgeon at the Hospital imeni S. P. Botkin, was through with her main job and after N. M. Dobrotvorskiy had completed his work day). The results of these tests were published in April 1933 in the form of two articles (authored by K. M. Vintsentini and N. M. Dobrotvorskiy): "Respiratory Function in Stratoplanes" and "Temperature Conditions Aboard Stratoplanes." Kseniya Maksimilianovna Vintsentini wrote about Nikolay Mitrofanovich as a major enthusiastic scientist and wonderful person.

N. M. Dobrotvorskiy was discharged from the ranks of the Soviet Army in 1936 due to worsening health, and subsequently continued to be very interested in problems of aviation medicine, processing an enormous volume of accumulated data.

At the very start of the Great Patriotic War, Nikolay Mitrofanovich went to the front as a volunteer. For some time he worked as deputy flagship physician in the Air Force, then changed to the post of chief of the health service of the aviation base area (RAB) in order to participate directly in medical support of combat operations of aviation units [chasti].

In his relatively minor job as chief of the RAB health service, Nikolay Mitrofanovich presented himself as a figure of enormous stature, and this was manifested primarily by the supreme authority that he enjoyed, not only on the part of physicians, but unit commanders, particularly, flight personnel.

During the Great Patriotic War, the airfield service battalions had infirmaries with small numbers of beds. N. M. Dobrotvorskiy stimulated in every possible way organization in these infirmaries of therapeutic and particularly surgical work, which made it possible to treat the sick and wounded, and consequently to save lives in their units. During quiet periods at the front, physicians at the RAB where N. M. Dobrotvorskiy was the chief of the

medical service were assigned to hospitals where they advanced their training.
There were reviews of complicated cases under the supervision of Nikolay
Mitrofanovich, and scientific-practical conferences were held. Not a single
opportunity was overlooked for specialization and advanced training of phy-
sicians and paramedical personnel. Much preventive work was done in the
units. Infectious diseases were extremely scarce among the personnel. In
the book, "Medical Service of the Air Force in the Years of the Great
Patriotic War," which was published in 1982, it is stated (p 136): "In
one of the airfield service battalions of the 15th Air Force, a passenger
bus was converted into an operating room at the initiative of the medical
service and with the active support of headquarters...." It was the initia-
tive of Nikolay Mitrofanovich, and only his unquestionable authority and
profound respect he enjoyed could influence the commander of the airfield
service battalion to outfit such a mobile operating room, which could
start to work quickly under any conditions.

Nikolay Mitrofanovich died at the peak of his creative talent. Poor health
deprived him of the ability to leave his house for the last few years. How-
ever, he continued to work hard: he wrote memoirs, systematized the accumul-
ated research materials in the field of aviation medicine and outlined the
possible routes of its development.

I. T. AKULINICHEV CELEBRATES HIS SEVENTIETH BIRTHDAY

[Article by editorial board]

[Text] Ivan Timofeyevich Akulinichev, doctor of medical sciences, professor,
active member of the International Academy of Astronautics, veteran of aero-
space medicine and medical instrument building, has celebrated his 70th
birthday.

I. T. Akulinichev, whose education was in medicine and engineering, became
one of the founders of medical radio electronics in the USSR.

His theoretical and practical contribution to medical instrument building
is universally recognized. I. T. Akulinichev created vector cardioscopes
that were brought up to broad industrial production, and he devised a number
of methods for functional tests in cardiology. His inventions in the field
of television engineering and in semiconductor circuitry, which had just been
conceived at that time, brought Ivan Timofeyevich wide renown in the USSR and
abroad.

The vast experience gained by I. T. Akulinichev helped him participate very
actively in preparations for and medical support of the first manned space-
flights, development of special telemetry equipment, coordination of bio-
medical instruments with the system of spacecraft control and telemetry,
expansion of carrying capacity of channels used for medical information. He
supervised research on development of methods and instruments for cosmonaut
training and monitoring their condition in flight. I. T. Akulinichev, as
a member of launching brigades, participated in all launches of Vostok and
Voskhod spacecraft. I. T. Akulinichev was awarded the Order of the Red
Banner of Labor and elected active member of the International Academy of
Astronautics for his work in medical support of spaceflights aboard the Vostok
series of spacecraft. He participated actively in preparations and implementa-
tion of the First Symposium of UNESCO in Paris (1962), and spoke well at
meetings of a number of astronautical congresses (Paris, Brussels, Madrid,
Tokyo).

In 1964, I. T. Akulinichev was awarded the International Prize and Christopher
Columbus Gold Medal for his work on use of radio electronics for humane

purposes. The work of I. T. Akulinichev dealing with optimization of relations between man and equipment in a man-machine system merits attention.

I. T. Akulinichev published several monographs ("Radio Electronics in Space Medicine," "Resonance Amplifiers on Lamps and Semiconductors," and others), more than 85 scientific papers and created 20 inventions. I. T. Akulinichev was repeatedly published in the leading press publications (PRAVDA newspapers and others) on timely problems of the role of science in modern society.

At the present time, I. T. Akulinichev continues to work fruitfully at the Institute of Introscopy, he is a member of several authoritative scientific councils and member of the editorial board of KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA. As far back as 27 years ago, he founded the section, Use of Radio Electronics in Biology and Medicine, in the Society imeni A. S. Popov. This section, which is headed by him to this day, has done much work in the ministries of the radio industry, electronics, instrument building, communications and others.

I. T. Akulinichev is industrious, modest and responsive, but at the same time he is irreconcilable with narrow-mindedness and superficiality in scientific research.

The editorial board of this journal and broad circles of specialists in space biology and aerospace medicine cordially congratulate Ivan Timofeyevich Akulinichev on his birthday and sincerely wish him good health, happiness and further creative achievements.

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